FOOD INDUCED ALLERGIC REACTIONS IN PEDIATRICS, WITH A RELEVANCE TO BEHAVIORAL VARIATIONS

A REVIEW

Submitted for Partial Fulfilment of the Master Degree
In Childhood Studies
Medical Department

By

ABOUL MAGD AHMED ABDEL REHEIM FARGHALY

M.B.B. Ch.

UNDER SUPERVISION OF

Prof.Dr. DIAIY HUSSEIN
Prof. of Pediatrics

Dr.OMAR EL SAYED EL SHOURBAGY
Lec. in Childhood Studies
Medical Department

INSTITUTE OF POST-GRADUATE
CHILDHOOD STUDIES
AIN SHAMS UNIVERSITY

1 9 8 8

وقل رب زدني علما

صدق الله العظيم

TO MY PARENTS , MY WIFE

AND CHILDREN

ACKNOWLEDGEMENT

I wish to express my deepest appreciation and profound gratitude to Prof. Dr. **DIAIY HUSSEIN** for his kind supervision and valuable advice which enabled me to finish this work in its present form.

I would like to extend my appreciation to Dr. **OMAR EL SAYED EL SHOURBAGY for** his valuable advice and continuous encouragement.

CONTENTS

LIST OF TABLES

CHAPTER 1

INTRODUCTION AND AIM OF WORK

INTRODUCTION AND IMPORTANCE OF THE STUDY

Allergic disease, which usually appears in childhood and is one of the most common reasons for pediatric visits, can become a life long problem. Allergy is one of the most common causes of acute and chronic disease in children. Over 20% of the pediatric population from birth to 17 years of age are allergic. Problems related to allergy account for nearly half of the outpatient visits in a busy pediatric practice. Allergy is the leading cause of school absenteeism in the United States, it is one of the main reasons for physical disability in children and often interferes with psychosocial development. It creates a serious social and economic hardships for family (Hein and Kishore,1984).

Food allergy is widely perceived by the public as a major health problem. Although the true incidence of food allergy is unknown, its incidence among children has been variously estimated from 0.3% to 7.5% and the incidence decreases with age.(Buckley and Metcalf,1982).

Historically, food allergy was first mentioned by the Latin Poet Lucretius in the 1 st century B.C. In modern times the importance of food allergy in childhood was recognised as early as the first decade of this century. In 1901, Hamburger documented the first case of Cow's milk hypersensitivity. The first report of allergy to egg occurred in 1912. An important achievement in this field was the classical experiment done by Prausnitz and Kustner, 1921 who transferred immediate sensitivity from his fish-sensitive co-worker Kustner to his own skin, demonstrating the presence of reaginic antibody in the serum of allergic patients. More than 40 years elapsed until IgE was found in the serum of hay fever patients and identified as a carrier of reaginic antibody activity (Businco et al., 1984).

Although some clinical aspects of cow's and goat's milk allergies were described by Hippocrates (570 -460 BC) and Galen (130-219 AD) respectively, the extent of food allergy remains uncertain in all age groups including early infancy (Wood,1986).

In 1906 pediatrician Von Pirquet introduced the term " allergy ", which is derived from the Greek word

allos, meaning change in the original state (Hein and Kishore,1984).

Food allergy may be expressed in one or more extraintestinal target tissues, The basis of the preferential reactivity of one system over another is unknown. The skin is a common target organ in food allergy. Skin reactions are evidenced by acute urticaria and/ or angioedema and much less frequently by chronic urticaria. Atopic eczema exacerbated by foods has been demonstrated in children. Asthma and rhinitis caused by food allergy are more common in children than adults. Systemic anaphylaxis as a result of allergy to ingested foods generally occurs within minutes but occasionally has been reported hours after ingestion of the offending food (Metcalf, 1984).

Gastrointestinal problems are prominent in infants where milk antigens are often incriminated. Entry of the offending foods into the stomach and subsequently into the intestine may result in nausea, cramping, pain, abdominal distension, vomiting, flatulence, and diarrhea. These symptoms of gastrointestinal involvement can be the only expression of food allergy(Metcalf, 1984).

Grant(1979) demonstrated that food allergy plays a major part in the provacation of migraine attacks. Monro and others (1984) concluded that observations confirmed that food-allergic reaction is the cause of migraine in their group study of patients.

Kittler and Baldwin,1970, had reported that food allergy can aggravate the behavioural dysfunction of children with " minimal brain dysfunction ". A combination of psychotherapy and allergy therapy improved the school performance and behaviour of a series of learning disabled children (Millman et al., 1976).

AIM OF THE WORK

Recognizing a need for information on food induced allergic reactions in children , we do this work to outline current knowledge in this area.

CHAPTER 2

DEFENITIONS

Definitions:

Food allergy is one of the more common forms of allergy and is especially encountered in early life, because incompletely digested foods tend to pass more readily into the circulation in infants (Mc Laren , 1981).

Allergy was originally defined by Von Pirquet (1906) as a specific change in the reactivity of an individual to a substance on the second or subsequent exposure to it. In 1931, Rowe described how allergy to foods eaten frequently could be masked and how it was possible to identify a food with particular symptoms only when it had been withdrawn from the diet and later reintroduced. Rinkel and his colleagues (1950), recommended a diversified rotating diet to prevent this type of allergy developing (Grant,1979).

Food allergy is defined as symptoms occurring locally, in the gastrointestinal tract, or in remote organs as a result of an immunological reactions. A patient may be said to have food allergy if he has a demonstrable sensitization, as shown by symptoms reoccurring on two or more occasions when a specific food is ingested; antibodies or antigen-reactive cells

can be shown to be present on such occasions ; and non-immunologic causes of adverse reactions have been eliminated. When the pathogenesis is uncertain, the general term **food intolerance** should be used. Food intolerance can also be due to a pharmacologic or toxic action. In addition, there may be " food idiosyncrasy " of the host, for which there is a non-immunologic mechanism, either based on enzyme defects or unknown causes (Businco et al., 1984).

Pearson et al (1983) defined food hypersensitivity as an organic adverse reactions to a food that is not due to its inherent toxic properties, and food allergy as hypersensitivity associated with evidence of an immunological reaction.

To standardize terminology, the American Academy of Allergy and Immunology Committee (1984) on Adverse Reactions to Foods had suggested definitions to be used in discussing aspects of food- induced reactions.

Food hypersensitivity (allergy) is defined as an immunologic reaction resulting from the ingestion of food or food additive. Adverse reaction to a food is a clinically abnormal response believed caused by an ingested

food or food additive. Food intolerance is a general term describing an abnormal physiologic response to an ingested food or food additive that is not proved to be immunologic in nature; category includes idiosyncratic , pharmacologic, metabolic, or toxic responses to food or food additives. Food anaphylaxis is a classic allergic hypersensitivity reaction to food or food additives involving IgE and release of chemical mediators. Anaphylactoid reaction to a food is an anaphylaxis- like reaction to a food or food additive as a result of nonimmune release of chemical mediators (Metcalf,1984).

CHAPTER 3

ROLE OF GENETIC IN FOOD ALLERGY

ROLE OF GENETICS IN FOOD ALLERGY

The burden inflicted by genetic forces in the development of human allergies is huge, if not overwhelming. Prospective clinical studies of 2- to 4-year old infants born to parents with atopy have shown that the risk for allergy approaches 50% to 58% in the presence of unilateral allergic parentage, and 67% to 100% with bilateral allergic parentage. The genetic mechanisms regulating IgE sensitization include both allergen-nonspecific (basal IgE production and generalized IgE hyperresponsiveness) and allergen specific factors(immune response and suppressor genes), (Zeiger et al., 1986).

Basal IgE production determined by serum IgE levels appears to be controlled by a two allele system (a dominant allele "R" and a recessive allele" r " in which a low serum IgE level is inherited as an autosomal dominant trait and a high serum, IgE level as autosomal recessive (Marsh et al., 1974). In the general population the " r " allele is common,represented by its calculated frequency of 0.49 to 0.52 (Rao et al., 1980).

Frequent penetrance of the recessive IgE alleles has been documented in twin studies in which genetic factors " alone " influenced 79% of the variation in basal IgE levels in children and 59% in adults(Bazaral et al.,1974) and in family studies in which 77% of offspring from high IgE matings exhibited high IgE levels compared with only 17% of offspring from low IgE matings (Gerrard et al., 1974).

The direct correlation of high maternal IgE levels to elevated newborn cord IgE levels and the continued elevation of infant IgE level when determined during childhood (Kjellman and Croner ,1984) attest to the strength of phenotypic expression of the " r " alleles for IgE production (Zeiger et al., 1986).

Influencing the hereditary regulation of basal IgE production are both allergen-nonspecific generalized IgE hyperresponsivenesss(linked to HLA-B8) and allergen-specific immune response and suppressor genes that are linked to several of the haplotypes in the HLA system.

Other variables that are likely genetic in nature, and will therefore strongly influence the individual

development of allergies, include but are not limited to mast cell/ basophil number, mediator content , and inherent releasability; IgE receptor number and affinity ; suppressive factor of allergy in relationship to inhancing factor of allergy; autonomic nervous system interrelationship to atopy, and target organ sensitivity (Zeiger et al., 1986).

Prenatal sensitization:

Nonspecific IgE produced by the fetus has been documented in human . As early as 11 weeks of gestation, IgE synthesis occurs in fetal lung and liver (Miller et al., 1973), and IgE can be detected in amniotic fluid at the 13 th week (Singer et al.,1974).

A placental barrier exists for IgE; therefore the presence of cord blood IgE represents fetal synthesis of IgE or contamination by maternal blood as in obstetric conditions that may lead to maternal-fetal blood admixtures (Allansmith and Buell,1964).

IgE cannot be demonstrated in arterial cord blood at any time of gestation or in venous cord blood before

37 weeks gestation, but it is detected in 20% of venous cord samples after 38 weeks and in 34% by term(Michel et al.,1980). Other investigators had also documented IgE in infant cord blood using paper radioimmunosorbent technique in about 13% to 82% of term pregnancies depending in part on atopic status of parents,maternal IgE, prenatal progestrone administration, and maternal helminth infection with microfilaria(Zeiger et al., 1986).

Specific IgE sensitization has been documented to occur prenatally to such allergens as pencillin, wheat, milk, egg , and microfilaria, specific prenatal sensitization to food and inhalent allergens is an infrequent event, occurring in about 1% of newborns (Croner et al., 1982).

In contrast, intrauterine infection with organisms capable of eliciting IgE responses, such as helminths, can trigger both nonspecific (82% of cord blood samples) and specific IgE (25% of cord blood samples) to microfilaria in the human fetus (Weil et al.,1983).

The effect of maternal diet during late pregnancy on the development of atopic manifestations in early infancy

in 212 infants of atopic families was recently examined. Mothers were randomized prenatally to a diet either avoiding cow's milk and egg, supplemented with Nutramigen and calcium (prophylatic group of 104 subjects) or of normal food (control group of 108 subjects). Postnatally, infants in both groups were encouraged to breast- feeding and supplemented with Nutramigen until the 3 months of age. There was no significant difference between prophylatic or control infants, respectively, in mean birthweight. Incidence of positive skin test resulted in (13% versus 21%), while atopic eczema or food allergy (5% versus 7%). These findings are consistent with infrequent occurrence of prenatal food sensitization and demonstrate that prenatal dietary avoidance cannot be expected to prevent atopy in infants of atopic families(Zeiger et al., 1986).

Postnatal sensitization:

Environmental modulation of IgE responsiveness postnatally may influence profoundly the eventual development of atopy. Nonspecific total serum IgE appears to be stimulated by exposure of T cell-deficient infants to formula feedings (Juto et al., 1982), infection with tissue phase parasites(Radermecker et al.,1974) and cigarette smoking (Kjellman,1981).

CHAPTER 4

MACROMOLECULAR ABSORPTION OF FOOD ANTIGENS

MACROMOLECULAR ABSORPTION OF FOOD ANTIGENS

During the neonatal period, the development of the mucosal barrier against penetration of bacteria, toxins and antigens is an important protective mechanism against a variety of pathologic conditions such as inflammatory and allergic reactions. The closure of the gut with regard to uptake of food antigens in a macromolecular form is determined by non-immunologic mechanisms as well as by the immunologic system of the gut.

Studies performed in humans showed that selective IgA deficiency, preterm delivery, intestinal helminth infection and type of feeding during the neonatal period might influence antigen uptake by the intestinal epithelium. These conditions, as well as various diseases affecting the gut, may cause increased absorption of intraluminal antigens and result in triggering of allergic type responses (Reinhardt,1984).

Intestinal absorption of intact food antigens in macromolecular form was suggested by Wilson and Walzerin, 1935. The intestinal uptake of food allergens is a necessary initial step in the development of a wide range

of allergic diseases, the mature gut absorps proteins in a biologically active and antigenically unchanged form (Bernstein and Ovary, 1968)and (Warshow et al., 1971).

In the fetal and neonatal intestine there is a high rate of uptake of macromelecules by enterocytes which are particularly important in animal species, which depend for their passive immunity on maternally transmitted immunoglobulins via colostrum during the first few days postpartum (Reinhardt, 1984).

There is an ample evidence that in most animals, intestinal uptake of macromolecules is maximal during the neonatal period and decreases thereafter,presumably because of the maturation of the intestinal mucosal barrier(Walker,1978).

The growth and maturation of epithelial cells, the functional maturation of the brush-border-associated enzymatic system, and the production of secretory IgA result in a functional gut closure to intact food antigens (Reinhardt,1984).

Experimental data suggested that hormones, enteric nutrient stimulation and factors present in colostrum contribute to the functional maturation of the intestine (Heird and Hansen,1977).

In the human, there is an indirect evidence of increased macromolecular uptake by the neonatal intestine (Rothberg,1969) , the intestine of healthy term infants is more permeable to food antigens during the first 3 months than later in life(Eastham et al., 1978). Structural and functional evidence of epithelial immaturity of the intestine has been reported in the human fetus and in preterm neonates (Maxey and Trier,1975).

Absorption of food antigens can occur at three levels: the membranous M-cells, the epithelial cells, and the intercellular junction(Reinhardt,1984), M-cells are characterised by a paucity of microvilli, a poorly developed glycocalyx and absence of lysosomal organellae. They are easily recognized by electron microscopy and are found to overlie the gut-associated lymphoid tissue in the ileum. Their structure and location make them ideal candidates for sampling food antigens in the intestinal lumen and presenting them to subepithelial

lymphocytes. It is a necessary step for the production of secretory IgA involved in immune exclusion of food antigens (Reinhardt,1984).

Uptake of macromolecules occurs also in epithelial cells of animals. The molecules are adsorbed to the luminal surface of cells, an invagination is formed resulting in the formation of small vesicles. The fusion of several vesicles gives rise to a phagasome and further fusion of phagasomes with lysosomes allows for intracellular digesion of the food molecules.

Undigested or partly digested breakdown products may be released into the interstitial space by the reversal of pinocytotic process, where they are presented to the subepithelial immune system or transported into IgA- or IgG- complexed form to the liver (Reinhardt, 1984). Fig."1" describe mechanisms for the uptake and transport of macromolecules by the intestine.

A widening of intracellular junctions due to disease or to surgical interventions on the gut may be a further reason for increased uptake of food antigens (Rhodes and Karnovsky,1971). Uptake of intraluminal antigen in a macromolecular form is estimated in normal

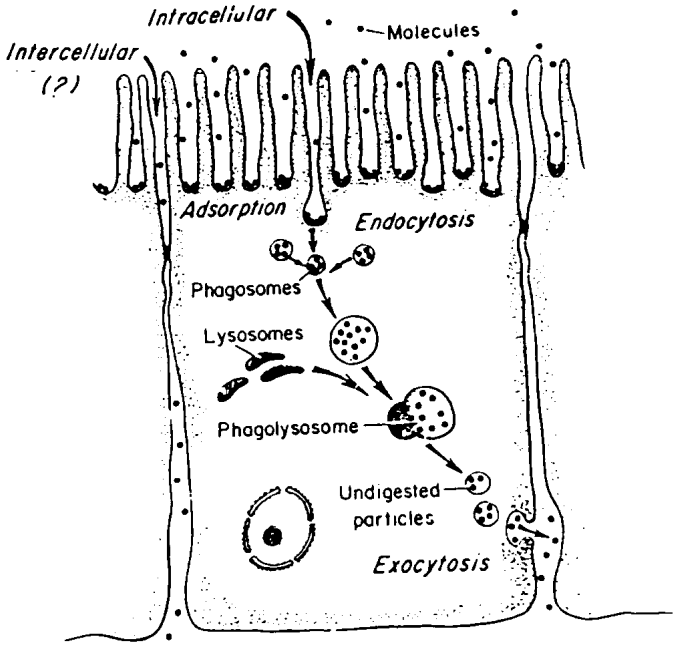


Figure 1 . General mechanisms for the uptake and transport of macromolecules by the intestine.(1)Intracellular uptake. After adsorption and endocytosis by the microvillus membrane, macromolecules are transported in small vesicles and larger phagosomes. Intracellular digestion occurs when lysosomes combine to form phagolysosomes. Intact molecules that remain after digestion are deposited in the intercellular space by a reverse endocytosis (exocytosis).(2) Intercellular uptake. Alternatively macromolecules may cross the"tight junction" barrier between cells and diffuse into the intercellular space.

(Cited from Walker and Bloch, 1983)

situation to be 2% of the total quantity ingested orally. In patients with selective IgA deficiency, this uptake is increased resulting in high levels of circulating antigen- antibody complexes(Rundles et al., 1979). In patients with atopic eczyma , gut permeability is similarly increased (Reinhardt,1984).

Immunologic mechanisms influencing macromolecular uptake

I-IgA: IgA system has a key role in immune exclusion of food antigens. Apart from exclusion dietary antigens, IgA can also be a surface receptor binding the antigen, facilitating its transport into the epithelial cell and thus allowing for intracellular breakdown and digestion in phago-lysosomes (Matthews,1974). Colostrum feeding stimulates production of secretory IgA in humans (Roberts and Freed,1977).

II-IgE : Antigen feeding induces under normal circumstances the generation of IgE-specific suppressor T-cells in Peyer's patches. In animals allergic to a food proteins ,IgE contributes to antigen-specific immune exclusion, but is also associated with antigen non-specific facilitation of macromolecular uptake of an unrelated bystander antigen (Roberts et al., 1981).

Studies performed on newborn infants have established an increased permeability of the gut for food antigens in preterm infants (Roberton et al., 1982). Gut closure appears to occur gradually with fetal maturation and is normally completed after 38 weeks of gestation. The maturation of the gut which allows for immune exclusion and intraluminal digestion of antigens is influenced by the gestational age but also by the type of feeding during the neonatal period (Roberts and Freed,1977). Children with heavy intestinal worm infection have a higher uptake of food antigens before treatment than after antihelminthic therapy (Reinhardt et al., 1983).

Reinherdt in (1984) showed that experimental animals as well as in humans, a wide variety of conditions may be associated with changes in antigen handling by the gut. Antigen may be taken up in an increased amount and have profound immunopathologic consequences. The neonatal period deserves particular attention.

In terms of macromolecular uptake, this is a period during which the infant is particularly vulnarable to antigens crossing the intestinal barrier which may switch

on the allergic response in newborns who are genetically at risk. Indirect evidence derived from circulating antibodies against common food antigens, suggests an increased passage of food antigens during the first 3 months of life (Eastham et al., 1978). During acute gastroenteritis, food antigen uptake in an increased amounts may give rise to sensitization and lead to allergic manifestations. In other situations such as protein deficiency or gut lesions due to helminth infection, passage of food antigens from the lumen to the submucosa may be a factor contributing to the immunopathology of these diseases (Reinhardt,1984). Fig "2" show hypothesis of interrelationship between gastroenteritis, cow's milk-sensitive enteropathy, IgA deficiency and lactose intolerance.

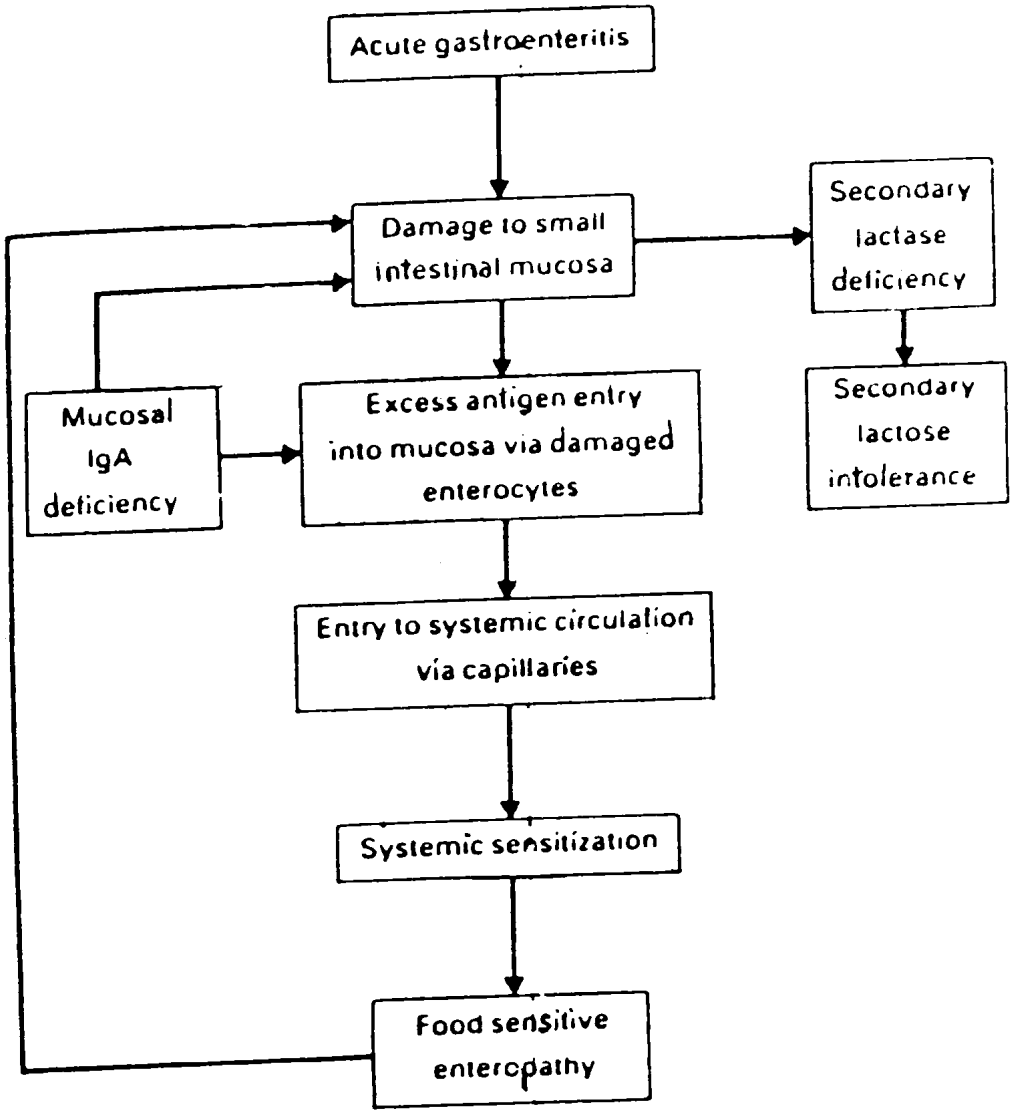


Figure 2. Hypothesis concerning interrelationship between gastroenteritis, Cow's milk-sensitive enteropathy IgA deficiency and lactose intolernace.

(Cited from Smith et al, 1984).

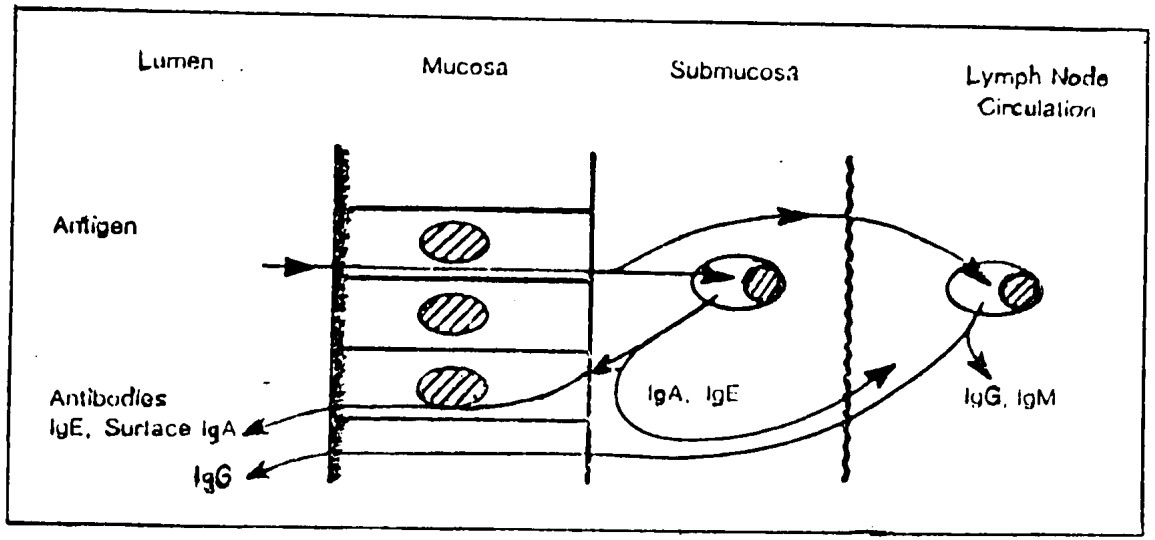
CHAPTER 5

PATHOPHYSIOLOGY OF FOOD ALLERGY

PATHOPHYSIOLOGY OF FOOD ALLERGY

Food represents the largest antigenic challenge confronting the human immune system. For sensitization to occur, it is necessary for such antigens to have contact with immunologically competent cells.(Sampson et al., 1987). There is abundant evidence that intact macromolecules of sufficient size to be antigenic pass through the epithelium of G.I.T. , interact with the mucosal immune system, and gain access to the circulation(Fig. 3) (Buckley and Metcalf, 1982). A number of factors determine the molecular size of dietary breakdown products. Ingested food is acted on sequentially by stomach acid and pepsins, pancreatic secretions, and intestinal peptidases. The mucosal endothelial cells actively absorb amino acids,small peptides, and intact proteins and the cellular lysozymes further degrade the proteins and peptides. Antigenic proteins and peptides traversing through Peyer's patches or the mucosal endothelial cells elicit an immune response, leading to active secretion of specific antibodies (prepondantly IgA) into the gut, which form complexes with their respective antigens, limiting further absorption of those antigens. Abnormalities in any of these processes can lead to an increased antigenemia, thereby exposing susceptible hosts to

Fig."3" Production of antibodies as a result of antigen passing through mucosal barriers



Cited from Buckley and Metcalfe, 1982.

sensitization. Achlorhydria, mucosal injury secondary to gastroenteritis, selective IgA deficiency and immaturity with relative IgA deficiency are examples of such conditions. (Sampson et al., 1987).

Additional factors that also influence sensitization, for example, individuals responding to food proteins with antigen-specific IgE are atopic and thus, in part, seem genetically predisposed to developing immediate reactions to foods (Sampson and Caskill, 1985). Fig."4" illustrate physiologic and pathological transport of antigens across the intestinal mucosa.

The majority of allergic reactions to foods are IgE mediated, mast cell-dependent and immediate hypersensitivity reactions. Such reactions have been transferred passively by intracutaneous injection of sera from allergic subjects into normal recipients ,followed by oral challenge with the corresponding antigen(Buckley and Metcalf,1982). When IgE is produced following sensitization by allergen contact, as appears to be the case in milk and egg allergy in infants, renewed contact with the allergen will frequently cause an immediate-type allergic reaction which depends upon the release of inflammatory mediators by mast cells and basophils (Weck,1984).

Mast cells, reportedly observed in gastrointestinal tissue as early as the third fetal month, gradually increase in number during infancy and childhood until adult levels are reached. While human skin contains , on the average, 7000 mast cells per cubic millimeter, the human duodenal mucosa contains approximately 10,000 to 20,000 mast cells per cubic millimeter (Metcalf,1984).

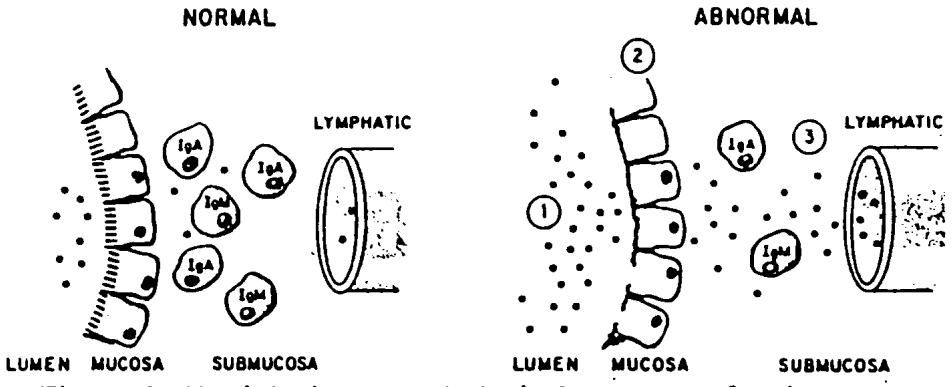


Figure 4 Physiologic and pathological transport of antigens across the intestinal mucosal barrier into the systemic circulation. Left: in normal conditions factors within the intestinal lumen on the surface of the epithelial cells and within the lamina propria combine to limit the access of antigens to the systemic circulation. Right: however, when these natural defenses are disrupted excessive quantities of antigenic material may enter the circulation and contribute to clinical diseases. Factors contributing to pathological absorption of antigens include: (1) decreased intraluminal digestion, (2) disrupted mucosal barrier or (3) decrease in IgA-producing plasma cells in the lamina propria.

Cited from Walker and Bloch,1983).

Mast cells in the GI tract mucosa reside primarily in the lamina propria, although occasionally mast cells are seen within the epithelial layer. Also mast cells are seen in the submucosa near small blood and lymphatic vessels (Lemanske et al.,1983). Human mucosal mast cells have been reported to degranulate in vitro in an IgE-dependent reaction. Food antigen-specific, IgE mediated, mast cell dependent reactions have reported in vivo after passive sensitization of nonhuman primate ileum and colonic mucosa. Local reaction could be induced after such passive sensitization by either ingestion or direct application of the antigen(Sampson et al.,1987).

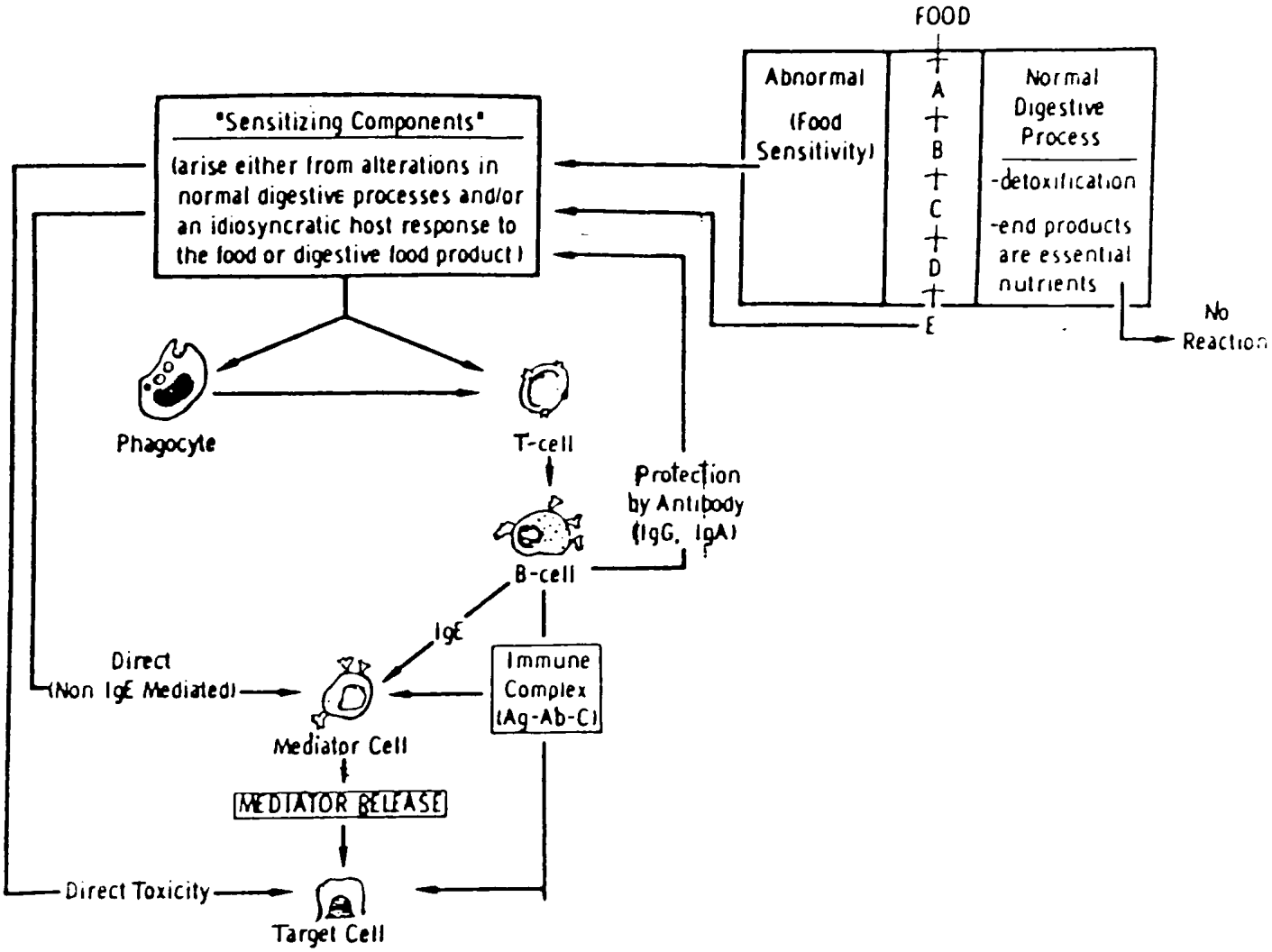
Mast cells degranulation results in the release of preformed mediators such as histamine, chemotactic factors, exoglycosidases, tryptic enzymes, heparin,and the generation of secondary mediators, including prostaglandins and leukotrienes. The immediate consequences of the release of these mediators from the mucosal and submucosal mast cells include a local change in vaso-permeability, stimulation of mucus production,increased muscle contraction, stimulation of pain fibres, and recruitment of inflammatory cells (Lemanske et al.,1983).

Studies suggest that when ingested food antigens encounter these IgE coated mast cells, degranulation occur, leading to increased goblet cell activity and increased mucus secretion, edema of mucosal epithelial cell villi, increased protein loss from the gut ,and increased absorption of foreign antigen. Intestinal biopsies performed in humans before and after food challenge have disclosed findings consistant with a similar course of events. Local intestinal anaphylaxis has been shown to facilitate the passage of macro-molecules through the GI tract barrier so that they may be distributed to other target organs, initiating degranulation of mast cells at those sites(Sampson et al., 1987). Such degranulation may be accompanied by an increase in plasma histamine (Sampson and Jolie, 1984).Fig"5" show a schematic representation of possible pathogenic mechanisms in food hypersensitivity.

Besides mast cells and basophils, other cells may be involved in immediate type reactions. Among the complex interactions which should be quoted are:

a) the activation of granulocytes by immune complexes that release proteases which in turn attack mast cells,

b) the activation of platelets either by platelet - activity factor or by IgE allergen complexes that



Fiture: 5 A schematic representation of possible mechanisms involved in food hypersensitivity.

(Cited from Bellanti, 1984).

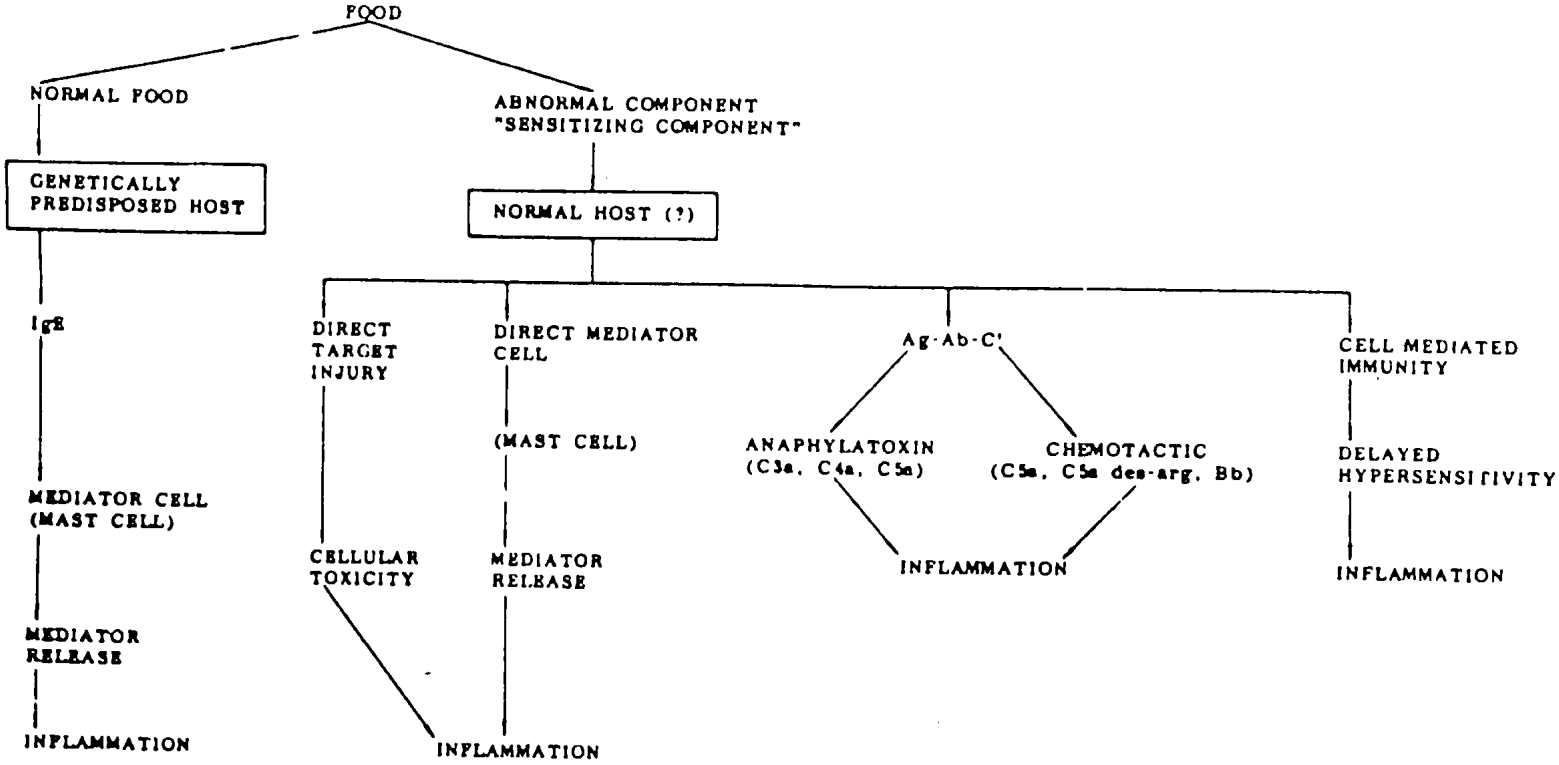
lead to the release of serotonin, and c) the activation of T-lymphocytes that lead to the production of lymphokines such as interferon which modulate histamine release by mast cells and basophils (Weck,1984).

While immediate hypersensitivity reactions can explain many reactions to foods, there is evidence that antigen-antibody complex-mediated mechanisms are also involved in milk and soy- induced gastroenteropathies. IgG and IgM antibodies to food determinants have been demonstrated both in GI tract secretions and serum (Kriebel et al.,1969). Interaction of food antigen with such specific antibodies may lead to complement activation. Complement deposition has been demonstrated in GI tract tissues. Complement activation within the bowel wall could be expected to lead to mast cell degranulation through generation of C3 and C 5a anaphylatoxins. Cytotoxic - type hypersensitivity reactions have not been documented in food allergy (Sampson et al., 1987).

Other triggering mechanisms for mast cells and basophils are the histamine releasing capacity of opiates, such as morphine or codeine. More relevant to food

allergy may be release induced by basic peptides, peptones, and possibly a number of food additives such as salicylates, sodium benzoates, tartrazine,etc. When not due to specific sensitization, such reactions should be called pseudo-allergic. They are very difficult to differentiate clinically from true allergic reactions, since symptoms are due to same mediators. But their evolution is usually more capricious, and they show a dose dependency which is not as strictly observed in allergic reactions (Weck,1984). Fig " 6 " is a schematic representation of events leading to mediator release, inflammation and cellular toxicity in the development of food allergy.

Figure. 6 Schematic representation of events Leading to mediator release, inflammation and cellular toxicity in the development of food allergy.



(Cited from Bellanti, 1984).

CHAPTER 6

IMMUNOCHEMISTRY OF FOOD ANTIGENS

IMMUNOCHEMISTRY OF FOOD ANTIGENS

Food contains many types of molecules, some of which cause allergic or pseudo-allergic reactions in some humans. The identification of the antigenic molecule in various foods and the type of allergic reaction they elicit is important for the satisfactory diagnosis in the individual patient and in the control of modified foods (Gjesing and Lowenstein,1984).

All food proteins taken via the oral route, are likely to be allergenic to some degree.Allergic disease caused by food allergens may take on a variety of forms depending on the organ (s) bearing the brunt of the reactions, the gut itself, the skin, the lungs, joints or entire body. Factors governing the severity of the disease include the level of sensitization, the antibody isotype, the type of allergic sensitivity and the extent of antigen absorption from the gut (Coombs and Mc Laughlan,1984).

The food we eat every day consists mainly of naturally occuring biological products. Additional compounds are added to improve the appearance and stability of the food. The final product, contains molecules that

cause allergic or psuedoallergic reactions in some humans.

A group of low molecular compounds can act as haptens. After combining with a carrier molecule they give rise to antibody formation and allergic reactions after sensitization. The initial sensitization can be caused by skin contact, for instances in nickle and chrome allergies. The haptens will also act as heptens after food intake in sufficiently sensitive patient . A group of compounds, without being antigens, produce the same symptoms as those seen in allergic patient. Some food colours, food preservatives, and other additives belong to this group. These biologic reactions are usually referred to as food intolerance or pseudo-allergic reactions. (Gjesing and Lowenstein,1984).

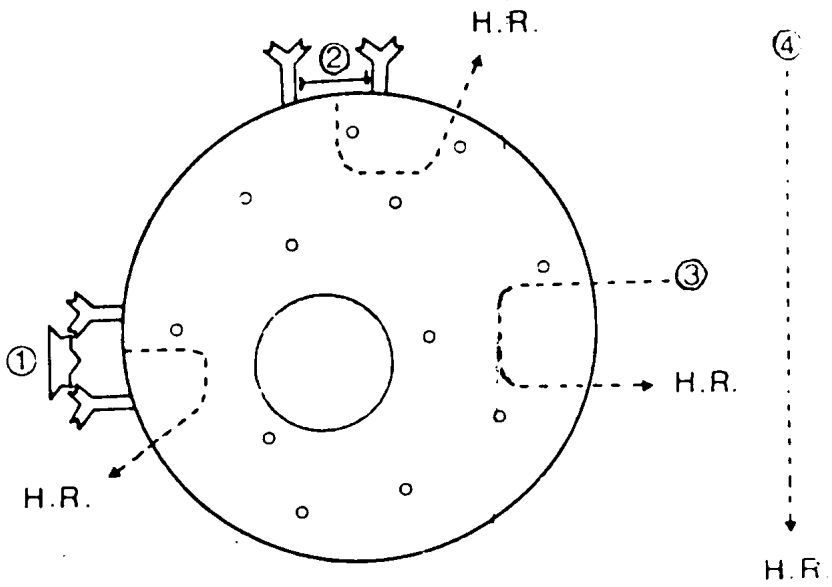
There are many reports in the early literature of antibody responses to milk and egg proteins taken orally. Today, all classes or isotypes of food antibodies may be satisfactorily measured by ELISA (enzyme-linked immuno-sorbent assay) with food antigens adsorbed on the walls of microtitre plate wells. In man, generalised type I sensi-tivity to food allergens, such as milk, egg or nuts, may be

shown by antigen -induced histamine release from blood basophils (McLaughlan and Coombs,1983).

Food allergic diseases are a potential consequence of the allergenicity of administered food proteins. The pattern of the disease depends, among other things, on : 1) the extent of allergic response or sensitization , 2) the antibody isotype in the antibody - mediated reactions, 3) whether " cell- mediated immunity " reactions are involved, and 4) the circumstances of the particular reactions, i.e. the type of reaction (type I-IV) and the organs bearing the brunt of the reactions, the so-called target-organ. The lungs are the major target-organ in food-induced asthma, the skin in atopic dermatitis. In some circumstances, the lesion and clinical manifestations are limited to the alimentary canal (mucosal changes in coeliac disease, colic and diarrhea associated with type I-gastrointestinal allergy) (Coombs and Mc Laughlan, 1984).

A schematic representation of the mast-cell with its possible reactions to different food compounds is shown in Fig. 7. (Gjesing and Lowenstein,1984).

Fig."7" Possible reactions between the mast cell and components of food .



Possible reactions between the mast cell and components of food.1) Antigen bound to specific IgE. 2)Lectin bound to the Fc-part of the immunoglobulin. 3)Trigger for histamine release.4) Histamine-like compounds.

(Cited from Gjesing and Lowenstein,1984).

Allergenicity of cow milk proteins :

This is the first protein rich food that most infants receive after weaning. They get this massive load of antigens at a stage when their immune system is not yet fully mature. All the known antigens of milk are proteins. Table (1), shows the major proteins of cow's milk and some of their physiochemical characteristics (Gjesing and Lowenstein, 1984).

Gunther and others (1962) studied serum antibodies to milk proteins giving passive hemagglutination in infants, one hundred and eight infants were followed from birth and the level of hemagglutinating antibody measured at intervals in either totally breast- fed infants or in infants receiving recorded bottle feeds. The antibodies to cow's milk developed very rapidly after birth (8-11 days). The degree of response to casein, α -lactalbumin and β - lactoglobulin varied from one infant to another.

Cow's milk consists of casein (80%) and whey proteins (20%), Beta lactoglobulin is the principal protein in whey , appears to be the most allergenic of the milk proteins, and is relatively resistant to heating

Table " 1 " Characterization of Some food Antigens

Source/Protein	MW x 10^3 monomeric forms	Pl	% Carbo-hydrate	% of total Protein
Cow's milk				
Casein	20-30	3.7-6.0		82
B-Lactoglobulin	18.3	5.3	0.1	9
α-Lactalbumin	14.2	5.1		3
Serum albumin	67	4.7		1
Lmmunoglobulin	160	5.6-6.0	2-12	2
Hen's egg white				)
Ovalbumin	36		1	)
Ovomucoid	27	3.9	22.9	) 75 %
Ovotransferrin	78	6.1		)
Wheat flour				
AG 23	24	6.5		
AG 7	52	5.0		

(Cited from Gjesing and Lowenstein, 1984)

and proteases. It is a glycoprotein with a molecular weight of 36,000 and contains two identical polypeptide chains, each with a molecular weight of 18,000. Other proteins in milk include alpha lactalbumin, bovine serum albumin, and bovine gamma globulins. Casein and beta lactoglobulin are synthesized in the mammary gland and do not appear to have a relationship to bovine plasma proteins (Metcalf,1984).

Infant milk formula have been exposed to varying degrees of heat and other treatment. Table (2) shows the continued presence of some milk proteins after boiling under varying conditions, as well as the presence of the same milk proteins in various milk infants formulae. Albumin and immunoglobulin are the most heat-labile antigens.

In the human digestive tract, milk is exposed to a range of proteolytic digestion processes at varying pH. There is successive disappearance with time of the different antigens when exposed to high pepsin concentration at pH 4.0 and 37°C. The reaction was stopped by adding sodium bicarbonate. Most of the antigens disappeared almost immediately while β -lactoglobulin was the most

Table 2 Presence of Antigenic Components in Various Milk Products*

	Heating Min	°C	Alb	AG 2	(Oroso-MUC.?)	β-lact.	AG 9	Lact. fer.	AG 15	α-lact.	Transfer.	Lac. per.	IgG IgA
Bovine whey			+	+	+	+	+	+	+	+	+	+	+
Mature bovine milk	2	100			+	+	+	+		+			
- - -	30	100			+	+	+	+		+			
- - -	60	100			+	+	+	+		+			
Pasteurized milk	0.25	75	+		+	+	+	+	+	+	+	+	+
Boiled skim milk	60	100	+		+	+	+	+		+			+
Skimmed milk			+	+	+	+	+	+	+	+	+	+	+
Allomin			+	+	+	+	+	+	+	+	+	+	+
Acidified allomin			+	+	+	+	+	+	+	+	+	+	
NAN			+	+	+	+	+	+		+			+
Nidina			+	+	+	+	+	+	+	+	+	+	
Babymin B			(+)	+	+	+	+	+	+	+	+	+	(+)
Nutramigen													
Pregestemil													

* + present; (+) reduced; and blank, not present.

(Cited from Gjesing and Lowenstein, 1984).

stable antigen under these experimental conditions. The infant food"Nutramigen " is a casein hydrolysate, it has been hydrolysed to such an extent that rabbit antibodies cannot precipitate the fragments(Gjesing and Lowenstein,1984).

Anderson and Co-workers(1979) showed in guina pigs that"evaporated milks " lost their capacity to sensitize orally to β-lactoglobulin, one of the main milk sensitizing proteins. The " evaporated milks " were also less sensitizing to casein.

The sensitizing capacity to β -lacto-globulin and casein was reduced as the heat-treatment became more intense and prolonged. An experiment was carried out on goat's milk, it was found that boiling reduced its sensitizing capacity to a greater extent than was with cow's milk. A special hypoallergenic milk formula is suggested (pregestimil and AL 110) and milk substitutes (Prosobee, soya-based product and comminuted chicken). After 37 days drinking pregestimil (a feeding formula based on predigested casein) no anaphylactic antibodies or sensitivity developed, While " AL 110" (a lactose free purified casein formula) was found to be sensitizing to casein but not to β-lactoglobulin.

Comminuted chicken and " Prasbee ", two alternative" hypoallergenic " cow's milk substitutes, sensitized 50% of the guina pigs to the product fed.(Mc Laughlan et al., 1981 a,b).

The low sensitizing capacity of "evaporated " or " liquid concentrated " milk formulae suggested that it should be possible, with selected heat treatment, to manufacture a fully nutritive milk product that is non-sensitizing and such investigations are presently in progress (Coombs and Mc Laughlan,1984). Kilshaw et al., 1982 reported that heat treated diafiltered whey failed to sensitize guina pigs. They suggest that this should be considered as a non sensitizing baby milk.

McLaughlan and Coombs (1983) showed that over 20% of infants under 6 months released more than 9% of their blood basophil histamine content in the presence of cow's milk proteins, while 10% showed a higher level of sensitivity (14-63% histamine release), while 37 % of the infants showed no release at all.

Hen's egg white:

Langeland (1982 a) described 13 different allergens among the total of 24 antigens seen as precipitates using rabbit anti-egg white antiserum

by the crossed immunoelectrophoresis (CIE) and by crossed radio- immunoelectrophoresis (CRIE) methods. The major allergens (Ovalbumin, ovomucoid and ovotransferrin) make up 75% of the total protein content of hen's egg white. They are described in table (1). Lysozyme, another protein of high concentration in hen's egg white, appeared not to be an IgE-binding protein in the CRIE system (Langeland, 1982b).

Ovalbumin and ovamucoid are the primary allergens in egg white protein. Both are present in uncooked and cooked egg. Conalbumin (ovotransferrin) is also allergenic.(Langeland and Harbitz,1983).

Individuals reactive to egg are usually sensitive to egg white. Egg yolk hypersensitivity is not usually reported in patients with egg allergy. Carrillo and his colleages (1986) described a 12 year old female patient with a medical history of urticaria, angioedema and severe acute bronchospasm shortly after the intake of small amounts of egg-yolk.

Wheat flour:

It is a food stuff causing food allergy in some patients. The gluten part can produce coeliac

disease or gluten intolerance (Gjesing and Lowenstein, 1984).

Blands et al (1976) studied an ammonium acetate extract (pH 8.2) of wheat flour and found 40 antigens, twenty of these antigens were present also in a rye flour extract, and six were also found in the gliadin fraction. Eighteenth antigens showed IgE binding when incubated with sera from 13 bakers allergic to wheat. Two of these allergens are described in table (1). Sutton et al (1982) fractionated wheat in albumin,globulin, glutenin,heat-treated , acid digested and other substances. They studied the sera from 20 allergic children with high levels of wheat-specific IgE as measured by wheat flour RAST. two of these children were described as definitely wheat-allergic, i.e. not tolerating wheat in their diet.

Kushimoto and Aoki,1985, reported six cases of masked type I wheat allergy in relation to exercise-induced anaphylaxis whether exercise induced urticarial reaction or exercise accentuated urticarial reaction to wheat. They prepared different allergens from wheat(glutin, gliadin, and glutenin) and showed that wheat allergens are reinforced in the stomach and destroyed by trypsin digestion in the jejunum.

Shash and Co-workers (1981) found that 22 out of 50 children with skin allergy (44%) showed positive skin tests to egg and milk proteins, whereas 28% of children(56%) showed negative skin tests to the same antigens. In the control group, 7 out of 50 children (14%) showed positive skin tests to the same antigens.

The higher incidence of positive reactions to egg and milk proteins in children with allergic skin disorders indicated that those patients have an increased level of specific IgE antibody in their skin. However, positive skin tests does not mean allergy, but it only reflects the immunological status of the children, which may explain the 14% positive reactions to skin tests among the control group. As regards the positivity to each antigen, they found that the highest, positive reactions were to bovine serum albumin (24%), then casein (20%), then alphalactalbumin (16%), then beta lactoglobulin (10%), whereas the lowest positive reaction was to egg albumin (8%).

Allergenic food proteins, although generally heat and enzyme resistant, may be altered by food preparation. Factors such as whether the food was raw,cooked or otherwise processed are of importance. Food antigens

capable of inducing allergic responses may be limited to only part of the food, such as the skin from an apple, or may only be transiently present at a certain stage of ripeness.

A suspected food may fail to consistently lead to an allergic reaction. Reasons for this inconsistency include the amount consumed, the presence of other ingested foods that delay digestion, the state of the food, and the possibility that concomitant medications such as antihistamines may have masked the reactions. It has been suggested that in some cases food reactions are noticed only when the individual is suffering from other allergic problems (Metcalf, 1984).

CHAPTER 7

EFFECT OF BREAST FEEDING ON ALLERGIC SENSITIZATION

EFFECT OF BREAST FEEDING ON ALLERGIC SENSITIZATION

A. Potential beneficial effects:

Breast feeding may decrease allergic sensitization by reducing both exposure and intestinal absorption to food antigens (Zeiger et al.,1986). Intestinal absorption of food antigens, caused by increased intestinal permeability , appears universal in human neonates, with absorption significantly greater in preterm than in term infants (Robertson et al.,1982). The protective role of human breast milk immunoglobulins, especially sIgA, in inhibiting absorption of antigenic substances has been documented in human neonates (Walker,1977). Breast milk control the transport of antigenic molecules into the circulation of newborns by inducing an earlier maturation of the natural intestinal barrier or by passively providing factors that promote such a barrier until such a barriers develop. Intestinal permeability to foods may naturally decrease with the maturing gut perhaps related in part to a maturing secretory IgA system (Zeiger et al.,1986). For example, salivary IgA can be detected in 92% of infants by 1 month, although still being low during the first 6 months after birth (Selner et al., 1968).

Infants and children with selective IgA deficiency manifest increased intestinal permeability because of the absence of sIgA and thereby showing augmented immunologic responses to foodstuffs including precipitins to milk (50%), bovine serum(23%), and fetal calf serum(23%)(Rundles et al.,1978). Although the increased intestinal permeability to food antigens that occurs early after delivery declines later in infancy, intestinal absorption of food antigens still occurs, albeit in reduced amounts in older children and adults (Zeiger et al.,1986). Fortunately, gastrointestinal permeability does not appear to be increased in most food-allergic, eczematous children aged 2 to 9 years (Dumont et al.,1984). Because of the continued absorption of low quantities of food antigens throughout life, potential sensitization of at-risk atopic individuals may occur at any age, although it is greatest within the first 3 years of life. Mothers who practice prolonged breast feeding would be expected to delay introduction of solid foods, use less day care assistance, and smoke less (Zeiger et al.,1986).

Delayed solid food feeding may in turn reduce eczema (Fergusson et al., 1981). Decreased viral

exposure may reduce the potential for respiratory illness, bronchiolitis, and infectious asthma , as well as, the potential for increased IgE sensitization (Frick et al.,1979), abstinence from smoking would eliminate the stimulatory effect of cigarette smoking on IgE production(Kjellman,1981),.

Two common factors apparent in the studies that suggested that breast feeding reduced allergic disease were prolonged breast feeding (> 4 months and preferably 6) and delayed solid food introduction (Zeiger et al.,1986). Immunologic parameters that were associated with breast feeding and delayed solid feeding included significantly reduced serum IgE levels at ages less than 4 months (Saarinen et al.,1979) and by one year(Chandra,1979). Infants with reduced T cell one month after birth demonstrated higher serum IgE levels and peripheral eosinophilia when fed cow's rather than breast milk(Juto et al.,1982).

Consistent with the occurrence of infant sensitization caused by early antigenic exposure, normal infants fed milk or soya formulae during their first 3 months of life developed higher levels of milk and soy serum agglutinins than did infants introduced to these protein antigens after 3 months of age (Eastham et al., 1978).

Zeiger et al (1986) concluded that a very brief breast feeding with early solid food introduction most likely provides no benefit for the reduction of allergies compared with cow's milk feeding and early solid food feeding. As previously noted, breast feeding for less than 3 months could not reduce allergic disease, but prolonged(six months or more) breast feeding without any cow's milk resulted in reduced eczema during the first 3 years (Saarinen et al.,1979).

As regards the relation between the type of feeding and skin allergy. Shash and his co-workers (1981), found that the children who are artificially fed have the highest incidence of positive tests with percentage of 66.6%, those who are fed on mixed-feeding have the percentage of 50%, while children fed on breast milk have the lowest incidence of positivity with the percentage of only 20%. They concluded that children fed on cow's milk are predisposed to develop allergy more common and earlier than those who are on breast milk.

B. Potential adversee effects of breast feeding:

Although studies suggest that prolonged breast feeding (probably best if solid feeding is delayed)

may reduce atopy, adverse immunologic events may be attributed to breast feeding. The passage or transmission of dietary substances consumed by the mother through breast milk may potentially sensitize her offspring (Zeiger et al., 1986). Egg antigen in human breast milk had been demonstrated early (Shannon,1921). Bovine milk protein has been identified in maternal breast whey by enzyme-linked immunosorbent assay for casein and β -lactoglobulin(Stuart et al., 1984). Wheat antigen has also been found by precipitin assay in maternal breast samples (Hemmings and Kulangara, 1978).

These observations establish the availability of maternally consumed dietary allergens in breast milk with the potential to sensitize at-risk offspring (Zeiger et al.,1986).

Atopic manifestations as atopic dermatitis (Gerrard,1979), angioedema (Asperen et al.,1983),rhinitis and gastrointestinal tract allergy (Asperen et al.,1983) have been described as early as one week in nondocumented, exclusively breast-fed infants (Zeiger et al.,1986).

These allergic symptoms were tested clinically by repeated maternal elimination and challenge

attempts and confirmed immunologically by immediate skin tests or RASTs on infants(Zeiger et al.,1986).

A few studies have warned of the potential risk of allergic sensitization in the breast-fed, allergy-prone infants in whom inadvertent,infrequent and small quantities of foodstuffs(e.g., cow's milk) are ingested (Kaplan and Solli,1979). Others have pastulated that small quantities or delayed introduction of food allergens such as cow's milk potentially could increase later sensitization in humans, as has been documented in animal models (Jarrett and Hall,1979).

Notwithstanding, Mellon et al.,1983, determined the effect of delayed cow's milk ingestion for one year on clinical and immunological parameters in infants of allergic parents after a strict food avoidance regimen, their findings strongly suggested that delayed cow's milk ingestion did not increase the risk of cow's milk IgE or nonspecific sensitization in infants of allergic parents.

C.Effect of soy feeding on allergic sensitization:

Johnston and Dutton (1966) demonstrated a significant reduction in asthma and perennial allergic rhinitis in soy versus cow's milk feeding regimens,but difference in eczema development or hay fever. Brown et al.(1969) and Kjellman and Johansson(1979) using clinical and immunological investigations of infants of bilaterally allergic parents failed to demonstrate any protective effect of soy versus cow milk feeding on the development of allergy in the first 3 years of life.The incidence of atopy was greater than 60% in infants by 3 years in both soy- and cow milk-fed groups. Mortimer (1961) and Peters (1965) showed that infant sensitization to soybean protein has been documented to cause anaphylaxis and asthma. Additionally, IgE antibodies to soy occur commonly in (67%) of children with IgE antibodies to milk(Dannaeus et al.,1977).

Present evidence would support the use of formulas less allergenic than soybean (i.e.,protein hydrolysates) for the purpose of preventing food-induced IgE-mediated disorders. On the other hand, soy-based formulas may be useful in the treatment of selected

infants with cow milk intolerance (Zeiger et al.,1986).

D-Effect of early solid feeding on allergic sensitization:

To minimize allergenic load, delayed solid-food feedings to atopic-prone infants has been recommended for decades. Reported studies noted a reduction in allergy in breast fed infants added solid foods later in the breast-fed than in the cow's milk-fed groups (Zeiger et al.,1986).

In an attempt to evaluate the effect of dietary patterns on development of eczema by 2 years, Fergusson and others (1981), found that parental atopy and solid feeding patterns were significantly related to eczema. Infants of atopic parents developed two and a half times the incidence of eczema when fed solid foods during the first 4 months compared with infants of non-atopic parents not given solid foods during this interval. A direct relationship was noted between numbers of solid foods introduced during the first 4 months and the incidence of eczema. In the subgroup of infants of atopic parents not receiving any solid foods for 4 months, the breast-fed infant's ratio of eczema was (12%) compared with (25%) in the cow milk fed group, suggesting some

benefit of breast feeding.

Kajosaari and Soarinen(1983) found that eczema developed by one year represented about 14% of atopic prone infants exclusively breast fed for 6 months compared with 35% in a similar group of breast-fed infants in whom solid foods were added at 3 months.

In contrast,Fergusson et al (1983) found that there was no indication that either breast feeding or patterns of solid feeding practices significantly affected development of asthma by 4 years. This latter finding is consistent with most studies implicating viral infections rather than foods as the cause of asthma in early childhood (0 to 3 years) (zeiger et al.,1986).

CHAPTER 8

SOURCES OF FOOD ALLERGENS AND FOOD ADDITIVES

SOURCES OF FOOD ALLERGENS AND FOOD ADDITIVES

A) Food Allergens:

Only a few of the hundreds of different foods consumed cause the majority of hypersensitivity responses (Sampson et al.,1987). Food antigens causing allergic reactions tend to be glycoproteins with molecular weight between 20,000 and 40,000 daltons (Metcalfe,1985). These proteins, although generally heat and enzyme resistant, may be altered in some instances by food preparation. Such factors as whether the food was raw, cooked, or otherwised processed may be of importance (Sampson et al.,1987).

In infancy and early childhood the proteins in cow milk and soy have been highlighted as the major cause of food allergic syndromes, although wheat protein, egg protein, rice, fish,chicken meat, and corn, as well as tomatoes, oranges, bananas and chocolates have been reported to produce gastrointestinal symptoms in some individuals.

It is clear, that there is not always a consistent association between an individual food and a particular symptom or symptom complexes. The classical example of this is provided by the varied responses seen to cow milk protein.Table" 3 " Furthermore,in the case of cow milk protein, the symptoms may change with increasing age in the one individual: diarrhea in infancy and, in the same child, asthma in later childhood.

Table " 3 " Clinical manifestations attributed to Cow's milk protein intolerance.

Symptoms	Syndromes
Gastrointestinal	
Vomiting	Immediate onset syndromes
Diarrhoea	Cow's milk sensitive enteropathy
Abdominal pain	Protein losing enteropathy
Rectal bleeding	Cow"s milk sensitive colitis.
Gross	
Occult	
Respiratory	
Nasal stuffiness and sneezing	Allergic rhinitis
Chronic cough	Bronchitis
Wheezing	Asthma
Skin	
Rash	Atopic eczema
Localized swellings	Angioedema
Secondary general effects	
Iron deficiency anaemia	
Hypoproteinaemia	
Thrombocytopenia	
Eosinophilia.	

(Cited from Smith et al, 1984)

In some individuals a single food , and even possibly a single food protein, may cause a syndrome of gastrointestinal allergy but in others it may cause clinical intolerance to multiple foods (Smith et al., 1984).

The incidence of gastrointestinal food allergic diseases is greatest in the first months and years of life and decreases with age. This is especially true for delayed onset reactions to food when there is food-induced small intestinal mucosal damage (Dannaeus, and Johonsson,1979). It remains uncertain whether gastrointestinal syndromes of allergic origin, causing small intestinal mucosal damage, exist in adult life. These gastrointestinal syndromes of early childhood appear to be temporary in duration (Smith et al.,1984).

Molkhou and Waguet (1981) performed a long-term open study to investigate the importance of food allergy as a cause of atopic dermatitis. Thirty-five children with atopic dermatitis, aged one to 15 years, took part in the study. One or more provoking foods were found in the majority of children, as follows: Egg(28 cases), cow milk (27 cases), chocolate (15 cases),Cereals(11 cases), fish (4 cases), orange (4 cases) and nuts (1 case).

In the last decade, a number of well designed studies have suggested that food allergy plays a significant role in urticaria (Juhlin,1981).

Truswell(1985) reported that urticaria may be provoked by foods through an IgE mediated food allergy, especially to egg (ovalbumin in the white of hen's egg), peanuts, fish, or cow milk, those may also cause anaphylaxis.

Based on skin sensitivity testing of 200 allergic children below the age of 8 years, the following percentage of allergy were determined for those foods: chocolate 19%, cow milk 15%, wheat or wheat products 26% orange 25%, strawberries 33% and codfish 45% (Barret,1983).

Examination of the controlled studies cited supports the conclusion that a fairly short list of foods is responsible for the vast majority of obectively confirmed reactions. This list includes cow milk, peanut, other nuts, soy , egg, wheat, and fish. Chicken which is commonly used in elimination diets, has been a problem for a few patients (Bock,1986).

Foods can precipitate some attacks of asthma in infancy but come well behind infections. The role of foods

in asthma diminishes during childhood and they are uncommon precipitants in adults. Eggs., fish, nuts, and chocolate are among the foods most likely to provoke asthma in children. Skin tests are usually positive, indicating that IgE is implicated (Truswell,1985). Infantile eczema is associated with high serum titres of IgE and often with multiple positive skin tests.

Statistically significant responses to skin tests have been reported in infants apparently sensitive to a food, for example, exacerbation after milk or improvement after withdrawal of egg. A controlled trial showed improvement in 14 out of 20 children with infantile eczema when egg and milk were removed. Breast feeding reduces the chance of eczema but only partly in babies with a strong atopic family history.(Truswell, 1985). Cow milk allergy can produce gastrointestinal bleeding or protein loosing enteropathy, eosinophilia may be present. Sensitivity to wheat gluten is the cause of coeliac disease with jejunal atrophy (Truswell,1985).

Plant food materials which have been found to cause significant food allergy are listed in Table(4) according to their botanical classification. The wide

Table"4" Plant foods that causes significant food allergy.

Order	Family	Plant
Glumiflorse	Gramineae	Corn, wheat,rye,oats,rice
Tubiforae	Solanaceae	Tomato,potato
Liliflorae	Liliaceae	Onion,garlic,asparagus
Rhoeadales	Cruciferae	Cabbage,broccoli,mustard cauliflower,brussel sprouts
Rosales	Rosaceae	Strawberry,raspberry,apples
Rosales	Leguminosae	Peas,Peanuts,beans,soya been
Campanulatae	Compositae	Lettuce,artichoke sunflower, Cucumber,squash,pumpkin.

(Cited from Wood, 1984).

Table"5" Animal foods that causes significant food allergy

Phylum	Subgroup	
Athropoda	Crustacea	Crabs,Lobsters,Shrimps
Mollusca	Lamellibranchiata	Mussels,oyster scallops
Chordata	Pisces;Osteichthyes	Bony fish
	Aves	Chicken,turkey,duck, hen's egg.
	Mammalia	Cow,goat,sheep, Milk of cow, goat

(Cited from Wood, 1984).

biological differences between the very large groups (phylla) are reflected in the fact that cross reactive sensitivity between shell fish and fish allergic subjects is by no means inevitable. It is of interest that those sensitive to hen's egg may tolerate chicken meat, and those sensitive to cow's milk may tolerate beef Table (5) (Wood,1984).

Because of some degree of cross-reactivity between antigens in various foods from the same family, the allergen load may need to be minimized by reducing or completely avoiding the intake of other members of that food family. Common examples of plant and animal food families are presented in Table (6).

Cross-antigenicity, varies widely among members of the same food family, for example, the cross antigenicity is strong between milks of cow and goat , but weak between cow milk and cow meat. From clinical experience, cross-antigenicity between various types of fish is much stronger than between various meats (Bahna and Furukawa,1983).

Aas (1978) used masked and capsule challenges in a group of 84 children aged 1 to 16 years, twenty patients

Table 6 Families of Cross-Reacting Foods

A. VEGETABLES

LEGUMES	MUSTARD	PARSLEY	POTATO	GRASS	LILY	LAUREL	SUNFLOWER
Beans	Broccoli	Anise	Chili	Barley	Asparagus	Avocado	Artichoke
Cocoa bean	Brussels sprout	Caraway	Eggplant	Corn	Chives	Cinnamon	Lettuce
Lentil	Cabbage	Carrot	Peppers	Oat	Garlic	Camphor	Sunflower
Licorice	Cauliflower	Celery	Potatoes	Rice	Leek		
Peanut	Mustard	Coriander	Tomato	Rye	Onions		
Peas	Radish	Cumin	Tobacco	Wheat			
Soybean	Turnip	Parsley					
Tamarind	Watercress						

B. FRUITS

GOURD	PLUMS	CITRUS	CASHEW	NUTS	BEECH
Cantaloupe	Almond	Grapefruit	Cashews	Brazil nut	Beechnut
Cucumber	Apricot	Lemon	Mango	Pecan	Chestnut
Honeydew	Cherries	Lime	Pistachio	Walnut	Chincapin nut
Melons	Peaches	Mandarin			
Pumpkin	Plums	Orange			
Squash	Persimmon	Tangerine			
Zucchini					

C. ANIMALS

MAMMALS (Meat/Milk)	BIRDS (Meat/Egg)	FISH		CRUSTACEA	MOLLUSKS
Cow	Chicken	Catfish	Salmon	Crab	Abalone
Goat	Duck	Cod	Sardine	Crayfish	Clams
Pig	Goose	Flounder	Snapper	Lobster	Mussels
Rabbit	Hen	Halibut	Trout	Prawn	Oysters
Sheep	Turkey	Mackerel	Tuna	Shrimp	Scallops

(Cited from Bahna and Furukowa, 1983).

exhibited respiratory and skin symptoms to cod fish ingestion, peas provoked skin and respiratory symptoms in 25 patients, nuts (all types including peanuts) elicited skin and bronchial symptoms in 29 subjects, egg white triggered skin and respiratory symptoms in 27 children, wheat produced unspecific reaction in one subject, cow milk produced skin and respiratory symptoms in 10 patients, beans elicited three reactions , and soy beans no reaction.

Purified allergens from a few very common foods, e.g., lactoglobulin, lactalbumin and casein from cow milk and ovalbumin and ovomucoid from hen's egg have been available for many years (Goldstein and Heiner,1970).

In recent years several investigators have isolated allergens from several other foods. The best known and most hihgly purified and characterized is allergen M from Cod (Aas,1978). Other work has been performed with cereal grains (Hoffman,1975), soybean (Moroz and Yang, 1980), peanut (Sachs et al.,1981), and sesame seed (Malish et al.,1981).

Hoffman and others(1981) isolated the major heat stable allergen of shrimp. The less stable allergens

could also be important in the contact urticaria and traces might still remain after cooking (Hoffman et al.,1979). Barnett et al.,1987, examined the specific IgE binding by protein extracts of 11 food legumes, including soybean by RAST and RAST inhibition. Cross-allergenicity was demonstrated to be most marked between extracts of peanut, garden pea, chick pea, and soybean. The results have important implications for selection of effective hypoallergenic diets and for the diagnosis of patients hypersensitive to foods.

Foods may be contaminated by other foods as well as contain a wide variety of substances that lead to reactions that may be confused with food allergy. Cross contamination of one food by another may take place before processing, during processing, and during food preparation. Mold contaminants are prominent in fermented food products such as cheese, dried fruits, yogurt, and wine. Insect parts can contaminate spices and other foods. Drugs, dyes, additives, bacteria , and bacterial products occasionally contaminate foods., Milk from cattle has been contaminated with bacitracin, penicillin, and tetracycline used to treat bovine diseases. The amount of natural salicylates in foods is small, and for that reason it is unlikely that they provoke problems even in aspirin sensitive patients (Metcalf,1984) .

A suspected food may fail to lead consistently to an allergic reaction, Reasons for this inconsistency include the amount consumed, the presence of other ingested foods that may delay digestion, the state of the food, and the possibility that medications such as antihistamines may have altered the reactions. While it is commonly believed that tomatoes and citrus fruits are frequent causes of immediate allergic reactions, there is no evidence to support this from controlled studies. Morever , the hives, which may be observed after ingestion of strawberries , have never been shown to have an IgE mediated basis (Sompson et al.,1987).

B)**Food additives:**

In industrialized societies a wide variety of additives and contaminants are found in processed foods that provoke adverse reactions (Sampson,1986). Intolerance to food additives manifests itself in three main clinical syndromes: chronic urticaria/ angioedema, asthma and aperiodic rhinitis. Rhinitis may be associated with either asthma or urticaria, the association of asthma and urticaria is very rare (Ortolani et al.,1984).

As the presence of these chemicals is not apparent in food stuffs, the relationship between ingestion

of the additive and manifestation of symptoms is not apparent in most cases. In the absence of a clear demonstration of an allergy, we must suspect an intolerance to food additives in every patient with a perennial or recurrent allergy-like syndrome(Ortolani et al., 1984).

In the United Kingdom approximately 270 additives are permitted and must be listed , with the other ingredients, in descending order of concentration. Principal kinds of additives include, with examples are:

a) Colouring: tartrazine,sunset yellow,erythrasine.
b) Preservatives: benzoic acid , sodium metabisulfite sodium nitrite.
c) Antioxidants : butylated hydroxyanisole, butylated hydroxytoluene.
d) Flavourings: menthol, quinine.
e) Emulsifiers :etc. (Wood,1986).

Sodium metabisulfite and related compounds are frequently found in fruit juices, wine, beer, and sprayed on mushrooms, vegetables, potato chips, and seafood to preserve flavour and prevent spoilage (Baker et al.,1981). Antioxidant properties of busulfites render oxygen unavailable to promote bacterial growth. Metabisulfite ingestion

has been shown to exacerbate bronchospasm, vomiting, and urticaria (Schwartz,1983). The exact mechanism provoking metabisulfite reactions is not known(Wood, 1986). Monosodium glutamate an additive frequently used in Chinese food, is known to induce wheezing in some asthmatics (Allen and baker,1981). Benzoates, butylated hydroxytoluene, and butylated hydroxy-anisole have been implicated in 11% to 15% of cases of chronic and recurrent urticaria (Juhlin,1981) .

These preservatives are fequently found in ready-made foods, bread, milk and potato powders, fats oils, margarine ,mayonnaise, jams, chocolate, soft drinks, and instant drinks (Juhlin,1980). Nitrites or Nitrates rarely cause gastrointestinal symptoms and have been reported to cause cyanosis (from metheamaglobinemia) in infants ingesting spinach or contaminated water(Sampson, 1986). Tartrazine is a yellow azobenzene dye reported to provoke bronchospasm in as many as 5% to 10% of asthmatics (Vedanthan et al.,1977). In a large series of patients with chronic urticaria, tartrazine was implicated as a causative factor in 18% of cases (Juhlin,1981).

Another dye, annatto, was implicated in about 10% of cases. Tartrazine and other azo dyes are frequently

used in soft drinks, juices, a wide variety of foods, and medications. The mechanism of action for the variety of tartrazine-induced symptoms is not fully understood (Sampson,1986). In aspirin-sensitive group, two of 18 (11%) patients developed urticaria after ingesting between 0.22 to 0.44 mg of tartrazine (the amount of dye contaminating a colorcoded capsule or pill)(Stevenson et al.,1986). The adverse reactions to food additives, like those to aspirin, do not appear to be allergenic (i.e.,IgE mediated) and they may not even be immunologic (Podell,1985).

CHAPTER 9

CLINICAL FEATURES OF FOOD ALLERGY

CLINICAL FEATURES OF FOOD ALLERGY

Immunologically mediated reactions to foods are expressed clinically by a diversity of signs and symptoms, ranging from abdominal pain to generalized anaphylaxis. These clinical expressions of food allergy are influenced by factors that include age of the patient, quality and quantity of food ingested, and type and extent of associated medical problems. An allergic reaction limited to the gastrointestinal tract may be expressed as nausea and vomiting, an allergic reaction in the skin by urticaria, angioedema, or atopic eczema, and a reaction involving multiple organs by anaphylaxis (Sampson et al.,1987).

I-Gastrointestinal Food Allergies:

Gastrointestinal food allergic syndromes may be divided into these syndromes which manifest quickly (within few hours) after food ingestion and these disorders in which the onset is delayed for many hours or days. (Smith et al.,1984).

A- Immediate onset reactions:

a) Acute anaphylaxis to food: Some proteins possess a peculiar attribute, when injected,to diminish rather

than increase the defence of the body against their harmful action, this is known as anaphylaxis (the reverse of a guard or protection). Schlossman in 1905 documented symptoms of acute shock in infants, after ingestion of a foreign protein, namely cow milk. Finkelstein, in the same year described a death cases due to cow milk ingestion in infancy.

It is now known that anaphylaxis results, in most cases, from a generalised immediate Ig-E mediated reaction following the introduction of a sufficient amount of antigen into a previously sensitized individual,releasing histamine and other biologically active mediators from sensitized mast cell(Smith et al.,1984). This phenomenon of an acute anaphylactic reaction to an ingested food represents the most severe example or one extreme of the clinical spectrum of gastrointestinal food allergy, but fortunately does not always result in death (Goldman et al.,1963).

It has been suggested by Parish and his colleage(1960) that the sudden infant death syndrome may be due to cow milk anaphylaxis, modified because it occurs during sleep. Also other foods , for example, wheat can cause anaphylactic reactions (Pudd et al.,1981).

b) **Immediate onset gastrointestinal symptoms:**

Cow milk allergy:

Some entirely breast-fed infants are sensitive to cow milk. Small amounts of cow milk given as a complement feed or in solids may lead to rapid onset of vomiting which ceases when cow milk is completely withdrawn from the diet. In some infants the lips and tongue may swell immediately upon contact with cow milk. This edema, sometimes associated with urticaria, develops in minutes and disappears in a few hours if no more milk is given. Such infants must have been previously sensitized to cow milk in some way, possibly in utero or more likely via the presence of cow milk in maternal breast milk (Smith et al.,1984).

As in all allergic diseases, a familial tendency to cow milk protein allergy has been reported. The estimated frequency in pediatric patients varies from 0.6 to 1.9%. It generally manifests itself within the first 6 months of life and is characterised by early onset diarrhea. The median age at onset was 3 months in 41 infants studied by (Businco et al.,1984). With chronic diarrhea due to cow milk protein allergy. Stools were watery and mucoid, sometimes bloody, often followed by severe and persisting vomiting, which is accompanied by pallor and shock. Colics also were frequent. When the condition is not recognised early ,

complications like failure to thrive and malnutrition ensue, often associated with hypochromic aneamia. In more severe cases, hypoproteinemia due to allergic gastroenteritis was seen. Symptoms such as eczema, asthma, rhrinitis, urticaria and , less commonly shock may also appear, as shown in table "7" (Businco et al,1984).

Hill et al (1986) performed a study on the manifestations of cow milk allergy in 100 young children with a mean age of 16 months . Three groups of patients were subdivided. Group 1 were 27 patients with predominantly urticaria and angioedematous eruptions developed within 45 minutes of ingesting cow milk, they had positive skin test reactions to milk and elevated total and specific IgE serum antibody levels. Group 2, 53 patients had pallor, vomiting or diarrhea between 45 minutes and 20 hours after milk ingestion, these children were relatively IgA deficient. The 20 patients in group 3 had eczematous or bronchitic or diarrheal symptoms.

Egg allergy: Vomiting within a few minutes to an hour after egg ingestion is characteristic of egg hypersensitivity. Diarrhea, abdominal pain and nausea may also occur (Smith et al.,1984). Skin and respiratory manifestations also occur and may be a more important part of the clinical

presentation than gastrointestinal symptoms (Ford and Taylor,1982). Egg hypersensitivity was first described by Schloss in 1911 ,RAST and skin prick responses to egg are usually positive and helpful in diagnosis (Smith et al.,1984).

Acute abdominal pain seems to be a particular feature of fish hypersensitivity (Mizami et al.,1977). Peanuts often produce immediate reactions of the oral mucosa as well as abdominal pain (Smith et al.,1984). Some individuals have gastrointestinal and other symptoms related to a wide variety of foods. Such patients have a number of immediate symptoms such as vomiting,urticaria or wheezing upon exposure to multiple foods. They often have an individual and family history of atopy, peripheral eosinophilia, elevated total serum. IgE, and positive RAST and skin tests to specific foods(Smith et al.,1984).

B)**Delayed onset reactions:** Delayed reactions after food ingestion are much more difficult to diagnose although the pathology is in general more site-specific. Here elimination of food followed by challenge is at the heart of the diagnostic approach (Smith et al.,1984).

a) **Food sensitive small intestinal enteropathies:**

Changes in the structure of the small intestinal mucosa in response to the ingestion of particular foods provides clear evidence of food-sensitive disorders involving the small intestinal mucosa. Cow milk, wheat, soy protein, fish , rice, egg and chicken meat have now all been shown to produce a food-sensitive enteropathy, table "8".There is often clear historic evidence that acute gastroenteritis may precede the development of food-sensitive enteropathy(Smith et al.,1984).
It is clear that there is a close association between post-enteritis enteropathy and food-sensitive enteropathy in early infancy, which came first is usually difficult to determine (Walker,1982).

Cow milk sensitive enteropathy:

Unlike the gluten-sensitive enteropathy of untreated coeliac disease, cow milk sensitive enteropathy is of variable severity on proximal mucosal biopsy, and patchy in distribution, it is also characterized by thin mucosa. The acute onset syndrome is characterized by the sudden onset of vomiting and diarrhea, which then become persistent. The gradual onset manifests as chronic diarrhea with

Table "7" Clinical Data of 41 infants with Chronic Diarrhea due to CMPA

Clinical data	Number of cases	%
Age at onset=3 months(median)		
Diarrhea	41	100
Failure to thrive	41	100
Vomiting	19	46
Blood in stools	8	19
Colics	6	14
Shock	5	12
Eczema	14	36
Asthma	4	9
Urticaria	1	2

(Cited from Businco et al, 1984).

Table"8" Transient Food Sensitive Enteropathies of Infancy

Cow's milk-sensitive enteropathy
Transient gluten intolerance
Soy-sensitive enteropathy
Fish-sensitive enteropathy
Rice-sensitive enteropathy
Chicken meat-sensitive enteropathy
Egg-sensitive enteropathy

(Cited from Smith et al, 1984).

failure to thrive. Diagnosis is based upon the typical small intestinal biopsy, and clinical response to a cow milk-free diet(Smith et al.,1984).

Soy-sensitive enteropathy:

Ament and Rubin (1972) described damage of the small intestinal mucosa which improved after withdrawal of soy protein from the diet. Perkkio and others(1981) demonstrated the close morphologic similarity between cow milk-sensitive and soy-sensitive enteropathy, soy-sensitive enteropathy may occur on its own or as a sequel to cow milk sensitive enteropathy.

Transient gluten intolerance:

Is a syndrome seen when a child with gastrointestinal symptoms and an abnormally small intestinal mucosa responds clinically and histopathologically to a gluten-free diet, but subsequently thrives on a normal gluten-containing diet . . In infants less than one year of age, transient gluten intolerance should be considered as a part of the differential diagnosis of an infant who develops gastro-intestinal symptoms when he first encounters wheat protein (Smith et al.,1984).

Recently infants have been described with food-sensitive enteropathies to fish,rice, chicken (Vitoria et al.,1982) and egg (Lyngkoran et al.,1982), diagnosed by serial small bowel biopsies related to dietary elimination and challenge. In all cases, intolerance to these foods was temporary and preceded by cow milk protein intolerance (Smith et al.,1984).

b)**Food sensitive colitis:**

Rubin (1940) described rectal loss of fresh blood which responded to cow milk withdrawal. Gryboski(1967) reported eight children with cow milk colitis, which was established by elimination diet and challenge, Diagnosis was established by evaluation of sigmoidoscopic appearances. The advent of safe colonoscopy and multiple mucosal biopsy even in early infancy has showed esinophilic or allergic colitis as an important cause of chronic bloody diarrhea in infancy (Jenkins et al.,1983). Even breast-fed infants whose mothers drink much cow milk may develop cow milk colitis. In food sensitive colitis there is usually a dense infiltration of esinophils in the mucosa with the lesion resolving with food elimination(Smith et al.,1984).

c)**Mouth,oesophagus and stomach:** Aphthus ulcers have been reported in up to 20% of the population (Graysowski et al., 1966). Dolby and Wolker (1975) have reported the successful

use of disodium cromoglycate for such ulcers but whether these are truly food allergic in nature is uncertain.

Forget and others (1978) described esinophilic infiltration of the oesophagus which may be food related. Also Katz and co-workers (1977) found esinophilic infiltration of the stomach with a history of food intolerance, response to food avoidance, and laboratory evidence of reagenic activity.

D-Esinophilic gastroenteritis is characterized by protein loosing enteropathy, peripheral esinophilia, and iron deficiency anemia secondary to gastrointestinal blood loss. The pathologic classification is confused, and not all reports clearly indicate that this disorder is a definite food allergic disorder (Smith et al.,1984).

E-Infantile colic usually refers to a picture of episodes of crying and restlessness due to presumed abdominal discomfort with eructation and flatulence. Many causes such as maternal anxiety or aerophagy distending the gut have been put forwards. Cow milk, egg and fish seem to be the foods most often incriminated (Smith et al.,1984).Several studies have suggested that cow milk protein ingestion

may cause colic in some patients (Hill et al.,1979).

F-Irritable colon syndrome and Crohn's disease: has been reported in adults. Food elimination can induce a clinical remission in the irritable colon syndrome and also in some patients with Crohn's disease. Whether thse represents food allergic disease is still uncertain (Smith et al.,1984).

II-Food allergy and respiratory diseases:

Both upper and lower respiratory tracts can be affected by food allergy. Manifestations of either may be due to food allergy (common in infants) or may result from the combined effects of food allergy plus another defects such as a gastroesophageal reflux, a congenital defect of the heart or tracheo-bronchial tree, immunodeficiency syndrome (isolated IgA or IgG_4 deficiency), or a concomitant inhalant allergy.(Heiner,1984).

Chronic rhinitis is the most common respiratory tract manifestation of food allergy (Heiner,1984). An early symptom of pulmonary involvement is recurrent or chronic coughing, with or without sputum product. Wheezing and reversible airway obstruction occasionally result from the ingestion of cow milk or other foods. Recurrent or chronic pulmonary infiltrates, even alveolar bleeding ,may occur. (Heiner,1983).

Foods can be an important factor in "idiopathic" pulmonary hemosiderosis, particularly in children. Baker's asthma is an example of food allergy induced by inhalation of food allergens. Allergy to inhaled foods usually occurs beyond infancy, it is largely IgE mediated (Heiner,1983).

Recurrent serous otitis media may be solely or partially due to food allergy. Large tonsillar and adenoid tissues may be caused or aggrevated by food allergies. Lower respiratory tract involvement is associated with a delay in onset of symptoms and with a larger quantity of allergen ingestion than chronic rhinitis.Respiratory manifestations of food allergy are shown in table "9"(Heiner, 1984).

Respiratory tract disease which is related to ingestion of cow milk most commonly has its onset in the first year of life. Immunological tests are helpful in providing an indication of excessive immunologic responsiveness to food proteins. High levels of IgE antibody are associated with immediate type reaction and these may include broncial asthma. Patients with hypersensitivity to milk sometimes show dramatic changes in total IgE or total IgG_4 levels associated with removal

and reinstitution of cow milk into the diet (Heiner, 1983).

Frier et al.(1969) noticed wheezing 20 hours after the administrations of 0.2 ml of milk in eight infants. Hemagglutinating and precipitating antibodies help in the diagnosis. Chetty(1982),reported a child with extrinsic allergic alveolitis due to food allergy.

III- Food allergy and skin diseases:

A major etiologic role for foods has been demonstrated in urticaria, atopic eczema and dermatitis herpetiformis. In some patients with urticaria,whealing occurs within minutes of the ingestion of a particular food. In most cases, this appears to be an IgE-mediated cutaneous mast cells degranulation i.e. a classical type I hypersensitivity response (Atherton,1984).

Allergic and allergic-type reactions from foods seen in the skin consist of atopic dermatitis, intense itching, urticaria, angioedema, exanthema, pompholyx and fixed eruption. Most often the mechanism is immediate type hypersensitivity. Sometimes type II,III and IV

Table "9" Respiratory Manifestations of Food Allergy

Rhinitis	Recurrent pneumonia
Chronic cough	Pulmonary hemosiderosis
Bronchitis	Upper airway obstruction
Asthma	Serous otitis media

(cited from Heiner, 1984).

Table"10" Symptoms and Signs Suggesting Food Allergy.

Nummular dermatitis on the face and extremities in small babies
Scaly dermatitis around the lips and eyes
Dry cheilitis
Oedema and dermatitis in the eyelids
Atopic erythrodermia
Acute worsening of atopic dermatitis with or without urticarial rashes
Unexpected intense itching in atopic persons.

(Cited from Hannuksela, 1983).

allergic reaction may also be involved.
Blotchy nummular type atopic eczema on the cheeks and extremities in small children is the most typical sign of food allergy. Scaly dermatitis and also oedema around the mouth and eyes also warrant search for food hypersensitivity(Hannuksela,1983). Table(10)

Atopic dermatitis: Allergens in different age groups are listed in table " 11 " (Hannuksela,1983).

In babies under one year of age egg, cow milk and fish are the most common allergens (Atharton,1980). Also , soy beans, peas,bananas and cereals are found to cause atopic dermatitis. The most common type of dermatitis from egg hypersensitivity is nummular dermatitis on the cheeks and extremities. Milk and fish cause more acute symptoms with urticarial rashes and angioedema. Soy beans and cereals tend to produce more diffuse dermatitis which often spreads into erythroderma (Hannuksela,1983).

Milk allergy disappear usually during the second year of life (Savilahti,1981). Egg is still the most important food allergen between 2-7 years of age, its significance diminishes with age and children going to school usually can eat food containing egg as an ingredient. Fish allergy

Table " 11 " Most Common Causes of Allergic and Allergic-type Food Reactions in Different Age Groups.

Age group	Causes
0-12	Egg, milk, Fish, soy bean, pea, banana
2-7 years	Egg, fish, apple, pear, plum, Carrot, celery, potato, paprika, tomato, spices, nuts
7 years	Fruits and vegetables mentioned above, nuts, spices, fish

(Cited from Hannuksela, 1983).

is found in any age group and the patients are very conscious of that. Even the smell of fish can cause intense itching and worsen dermatitis(Hannuksela,1983).

Hypersensitivity to cereals is rare in older children but it occurs in some extent at any age. Erythrodermic atopic dermatitis warrants investigations for cereal allergy(Hammar,,1977). Apple, pear, plum, carrot, celery, swede, paprika and potato as well as various spices are the newcomers inthe list of common food allergens in older children(Hannuksela and Lahti, 1977). In teen agers and young adults the allergens are the same as in older children.

Citrus fruits and chocolate are added in the lists of food allergens. They often produce tiny vesicles on the palms and fingers and also intense itching and worsening of atopic dermatitis (Hannukesla,1983).

Urticaria is characterized by the appearance of transient cutaneous wheals generally lasting less than 24 hours. Angioedema is simply the subcutaneous counterpart of urticaria. Contact urticaria is a common condition in young children. The lips become swollen within a few minutes after contact with the causative food, particularly the skin

on the face and fingers. Foods may have two different aspects in relationship to urticaria, first, the relationship is a clear one and the urticaria appears within minutes of ingesting food, foods of this type includes eggs,milk,nuts,fish,shellfish,yeast, and strawberries, it is generally assumed that these reactions are IgE mediated. There are some evidence that certain foods, such as strawberries, may contain substances able to degranulate mast cells in a non-immunologic fashion. Other foods may provoke urticaria simply because of their high content of histamine (Atherton,1984).

Atopic eczema is an extraordinarily common disease among children, and one which can cause very real distress. It appears to be rather uncommon during the first 4 weeks of life, its incidence is very high in the next few weeks, so that about half of all cases will have appeared by the fourth month and 75% by the end of the first year (Atherton,1984).

For many years,there were reports of effective treatment of established atopic dermatitis by the dietary elimination of certain foods, particularly egg and milk (Juto et al.,1978).

Finally table"12" illustrate manifestations of food allergy

Table " 12 " Manifestations of Food Allergy

Gastrointestinal	
Vomiting	Protein-Loosing enteropathy
Abdominal pain	Enterocolitis
Diarrhea	Infantile colitis
Steatorrhea	Ulcerative colitis
Malabsorption	Proctalgia
Intestinal bleeding gross/occult	Refusal of milk
Constipation	Stomatitis
	Edema of lips
Respiratory	
Rhinitis	Recurrent pneumonia
Chronic cough	Pulmonary hemosiderosis
Bronchitis	Recurrent respiratory infections
Asthma	Upper airway obstruction
	Serous otitis media
Dermatology	
Atopic dermatitis	Perianal rash
Urticaria	Purpura
Angioedema	Dermatitis herpetiformis
Contact rash	Alopecia
Haematology	
Hypochromic anemia	Thrombocytopenia
Hypoproteinemia	Eosinophilia
Neurologic and behavioral	
Allergic tension-fatigue syndrome	
Urinary	
Enuresis	Orthostatic albuminuria
Cystitis	Nephrotic syndrome
Cardiovascular	
Anaphylactic shock	Cor pulmonale
Coronary heart disease	Cardiac arrhythmias
Miscellaneous	
Recurrent infections	Infantile cortical hyperostosis
Failure to thrive	Occular allergy
Sudden infant death syndrome	

(Cited from Businco et al, 1984).

CHAPTER 10

FOOD ALLERGY AND BEHAVIORAL VARIATIONS

FOOD ALLERGY AND BEHAVIORAL VARIATIONS

Food has been reported to affect behavior by altering the levels of central nervous system neuro-transmitters (Wurtman,1983) or by direct actions of psychopharmacologic agents in foods (as Caffeine). Indirect effects of foods on behavior via immunologic or allergic mechanisms have been postulated but the evidence available is not yet clear or convincing (Crayton,1986).

The known and postulated effects of food on behavior have stimulated interest in the possibility that adverse reaction to foods might contribute to the development of mental illness such as schizophrenia and depression (Crayton,1986).

Dohan and others (1984) suggested that wheat ingestion in genetically predisposed individual may aggravate schizophrenic symptoms and may even be a cause of schizophrenia. Singh and Kay (1976) reported cases of apparently wheat-sensitive schizophrenic individuals. The incidence of antigliadin antibodies in schizophrenics is higher than that in nonschizophrenic (Crayton,1986).

Recently Jansson and his colleages (1984) described a patient with schizophrenia who dramatically improved on gluten-free diet. Nasr et al (1981) have reported a high incidence of allergy in depressed patients, the incidence of allergy was about 33%.

Rix et al(1984) attempted to determine the incidence of food allergy in allergy clinic patients with psychologic complaints , 10 of their 18 subjects were diagnosed as having depressive neurosis. Perhaps the most commonly encountered type of patients with complaint of food sensitivity and behavioral symptoms will prompt a consideration of the somatization disorders (Crayton,1986).

May(1984) had pointed out the remarkable similarity between neurotic symptoms and the allergic tension-fatigue syndrome. Also, Randolph (1947), proposed that many patients diagnosed as neurasthenic were more accurately described as suffering from allergic-tension fatigue. Both are characterized by fatigue, irritability, depression, difficulty in concentration, and a wide variety of physical complaints.

1.Allergic tension fatigue syndrome:

Speer,1954, described the " allergic tension fatigue syndrome " which comprised tension and fatigue,alternating, restlessness and night mares, depression, manic hyperactivity and nervous fits. Abdominal pain, headache,nasal congestion and infra-orbital circles due to nasal venous congestion and pallor were also reported. Elimination of cow milk, chocalate, cola, corn, wheat, egg, was said to result in improvement.

Wood(1984) concluded that attempts to reproduce such delayed symptoms, which by their nature may be both delayed and ill-defined in double-blind crossover studies, the results were not impressive.

2.Hyperactivity and poor attention span:

Most studies of relationships between food sensitivity and childhood psychiatric disorders have carried out with children who have what is currently termed " attention deficit disorder ". Minimal brain dysfunction,hyperkinesis, and learning disability are among the terms formerly used for this group of patients (Crayton,1986). Attention

deficit disorder is characterized by " developmentally inappropriate attention, impulsivity, and hyper-activity ". Several articles suggest a relationship between food sensitivity and attention deficit disorder (Crayton,1986).

Hughes (1978) indicated that transcallosal-evoked potential latencies dropped from more than 70 m.sec. to under 20 after the institution of a hypoallergenic diet in food- sensitive children with learning disabilities. The report suggested that interhemispheric communication was dramatically slowed in some food-sensitive, learning disabled children.

Hyperactivity and poor attention span are associated with distractability and excitability, which lead to serious social and educational problems affecting perhaps 5% of preschool and school childrem, with a male to female ratio of 6:1(Wood,1984).

Kittler and Baldwin(1970) have reported that food allergy can aggravate the behavioral dysfunction of children with " minimal brain dysfunction ".

A combination of psychotherapy and allergy therapy improved the school performance and behavior of a series of learning-disabled children(Millman et al.,1976).

The theory that salicylates and artificial food additives cause hyperkinesis was first presented by Feingold(1975) who stated that hyperactive behavior and learning disorder of children might be a result of intolerance to the natural salicylates in certain foods which are similar in structure to the acetyl salicylate in aspirin. Some artificial flavors such as mint contain a salicylate radical. Based on this he constructed a " salicylate-free diet " which excluded foods containing natural salicylates, seven artificial flavors and all forms of aspirin.

A typical example of this diet is " Kaiser-Permanente Diet " exclude: 1) all artificial synthetic colores and/or flavors, 2) two vegetables (cucumbers,prunes) tomatoes) and 21 fruits (e.g. apples, grapes, oranges prunes) which contain natural salicylates, 3) certain non food items such as mouth wash, toothpaste , cough drops, lozenges, antacid tablets, perfume, gum and some drugs containing artificial flavors or colors. The diet was prescribed to children with hyperkinesis-learning disabilities.

Feingold (1975) reported improvement in about 50% of his patients. On other hand Ribon and Joshi (1982) concluded that hyperactivity leading to learning disorder of school-aged children is not improved by removing salicylates and food additives from the diet.

The harmful effect of food colors on behavior that has been noted within one half to three and a half hours after ingestion of synthetic colors is dose-dependent and is a toxic rather than an immunologic response (Ribon and Joshi,1982).

Harley et al (1978) concluded that such substances did not contribute to the syndrome in children of school age, although in the preschool child, teacher and parent alike agreed that some ameloration of symptoms occurred during the diet period.

In a selected group of 76 hyperactive children, 48 foods were implicated in doubly blind challenges and their elimination resulted in improvement in 62 children, of whom 21 returned to normal. The IgE levels were more than 100 u/ml in 68% of those

responding and in 20% of those who did not. Among food materials against which children with hyperactivity reacted cow milk, soy milk, chocolate, grapes, wheat,oranges, cheese and hens egg were prominent. Particularly common too were reactions to food additives(Egger et al.,1985).They prefered the hypothesis of allergy, but allergy and idiosyncrasy could co-exist and be interrelated in a complex manner. They concluded that the sequential reintroduction of foods enabled them to identify the foods that adversely affected a child's behavior. The hypothesis that combinations of any foods can alter behavior (based on allergy theory) has been supported in double blind controlled trials, not only in the hyperkinetic syndrome but also in migraine (Egger et al.,1983).

3-Food allergy and migraine:

Migraine is a multifactorial disease which may be induced through the ingestion of large amounts of chemical mediators in some individuals(Hanington,1971), or through an allergic reaction to foods in others(Monro, et al., 1980). In the latter group the exact mechanism by which foods cause the migrainous attacks is not clear. Monro et al(1984) had shown that migraine in some patients could be relieved by dietary exclusion. They demonstrated

that formal food-challenge can also provoke migraine and that pretreatment with oral sodium cromoglycate exerts a protective effect. They suggested that a food-allergic mechanism gives rise to symptoms in these patients. Their sensitivities to various foods were demonstrated by means of elimination, challenge, and positive intra-dermal testing.

Egger et al(1983),demonstrated that 93% of 88 children with severe frequent migraine recovered on oligo-antigenic diets, the causative foods were identified by sequential reintroduction and the role of foods provoking migraine was established by a double-blind controlled trial in 40 of the children. Most patients responded to several foods, suggesting an allergic rather than an idiosyncratic (metabolic) pathogenesis.

Associated symptoms which improved in addition to headache included abdominal pain, behavior disorder, fits, asthma,and eczema. The oligoantigenic diet consisted of one meat(lamb or chicken),one carbo-hydrate (rice or potato), one fruit (banana or apple), one vegetable (brassica), water, and vitamin supplements, for 3 or 4 weeks, depending on the frequency of headaches. Cow milk caused symptoms in most children. All but 1 of

those reacted to cheese, whereas 13 reacted to cheese but not to cow milk. Sheep-milk and goats-milk cheese given to those who had reacted to cow milk cheese, caused no symptoms. They suggested that the high prevalence of other atopic disease in the children and their first-degree relatives and the high frequency of positive skin-prick tests support the view of allergic disease rather than metabolic idiosyncracy. Table"13" illustrate 55 foods provoked symptoms.

Grant(1979) demonstrated that 60 migraine patients completed elimination diets after a 5 days period of withdrawal from their normal diet. When an average of ten common foods were avoided there was a dramatic fall in the number of headaches per month,85% of patients became headache-free. The commonest foods causing reactions were wheat 78%,orange 65%,eggs 45% , tea and coffee 40% each, chocolate and milk 37%, beef 35%, and corn, cane suger, and yeast 33% each. He concluded that food allergy plays a major part in the provocation of migraine attacks,.Both immunological and non-immunological mechanisms can cause food intolerance and both seem to be involved in migraine pathogenesis.

When antigen-antibody reactions occur on the surface of mast cells,5-hydroxytryptamine, histamine

Table " 13 " Number of children in whom foods caused symptoms

Food	n	Food	n	Food	n	Food	n
Cows' milk	27	Soya	7	White wheat flour	3	Vegetable oils	2
Egg	24	Tea	7	Artificial milk Substitute	3	Lentils	2
Chocolate	22	Oats	6	Banana	3	Peas	2
Orange	21	Goats'milk	6	Strawberries	3	Ice Cream	2
Wheat	21	Coffee	6	Melon	3	Rabbit	1
Benzoic acid	14	Peanuts	5	Carrots	3	Dates	1
Cheese	13	Bacon	4	Lamb	2	Avocad	1
Tomato	13	Potato	4	Rice	2	Rhubarb	1
Tartrazine	12	Yeast	4	Malt	2	Leek	1
Rye	12	Mixed nuts	4	Sugar	2	Lettuce	1
Fish	9	Apple	4	Ginger	2	Cucumber	1
Pork	9	Peaches	4	Honey	2	Cauliflower	1
Beef	8	Grapes	4	Pineapple	2	Mushrooms	1
Maize	8	Chicken	3			Runnet beans	1

(Cited from Egger et al, 1983).

and other vasoactive substances which can cause headache are released. Members of the grass family, including wheat, corn and cane sugar, are commonly found to be antigenic,78% of the patients tested in his study reacted to wheat. Significant elevations in IgG, IgA, and IgM have been found in migraine patients, and in some patients complement activation has been shown at the onset of headaches induced by exposure to known antigens.

Grant(1979) reported that the prognosis appears to be excellent for the patient whose migraine attacks are provoked by a few foods only, but widespread food intolerance can indicate underlying immunological and hepatic dysfunction.

CHAPTER 11

DIAGNOSIS OF FOOD ALLERGY

DIAGNOSIS OF FOOD ALLERGY

The diagnosis of food allergy starts with a careful history. The use of skin and radioallergosorbent test(RAST) assist in the clinical diagnosis. Confirmation of the diagnosis, when required and when judged safe,can only be obtained by double-blind or single-blind,placebo-controlled oral challenge with suspected foods(Sampson et al.,1987).

History:

The clinical history should include a detailed description of the specific symptoms from onset of illness to the present, with notations of the time between ingestion of food and onset of symptoms, a description of the most recent reactions, and an estimate of the quantity of food required to produce this reaction. The history should include specific details about grwoth and development and the age at which each food was introduced into the diet, as related to the onset or exacerbation of symptoms. Family history should record food reactions in parents, grandparents, siblings, and first cousins, as well as history of atopic diseases in close relatives.

Detailed information should be obtained concerning the physical and psychosocial environment of the patient. Cultural and religious attitudes about food should be noted. Inquiry should be made as to the existence of other atopic diseases including atopic dermatitis, asthma, and allergic rhinitis and to the agents that incite these problems. Pruritus, hives, eczema, angioedema, abdominal pain, nausea, vomiting, diarrhea, asthma, hypotension, and rhinitis are several symptoms and signs that may occur with the same food on different occasions.

As with the case of allergy to any food, the diagnosis of allergy to milk rests mostly on clinical grounds more than on laboratory tests. The diagnosis is suggested by a careful history taking and is verified by documentation of improvement of symptoms, after milk elimination from the diet and their recurrence on resumption of milk intake. Milk allergy should be suspected in infants with chronic or recurrent gastrointestinal, skin or respiratory symptoms and in those with unexplained hypochromic microcytic anemia. A positive family history of cow milk allergy may be a valuable clue to suspect milk as an offending allergen.Table" 14 " illustrate the diagnosis of cow's milk hypersensitivity.

Table "14" Diagnosis of Cow's Milk Hypersensitivity.

1. Medical History
   - Nature of symptoms
   - Age at onset
   - Feeding history
   - Relation of symptoms to milk intake
   - History of allergy
   - Family history of allergy, particularly to milk

II. Pysical Examination
   - Manifestations of allergy
   - Manifestations of nonallergic disease

III. Laboratory Test:
   1. To exculde or verify nonallergic disease
   (e.g.CBC,urine analysis,Stool analysis,Cultures,Radiologic studies Immunologic screening,Sweat electrolyte. etc.)
   2. To support diagnosis of allergy
      - Eosinophilia in circulation or local secretion of shock organ.
      - Serum IgE level
   3. To screen for causative allergens
      a.Most commonly used tests
        - Skin testing
        - Radioallergosorbent test (RAST)
      b. Less commonly used tests
        - Specific serum antibodies of IgG,IgM,& IgA classes (Enzyme-linked immunosorbent assay.Fluorescent immunosorbent test. Precipitation.Hemagglutination, Complement fixation)
        - Immune complexes in circulation or shock organ
        - Leukocyte histamine release
        - Leukocyte migration inhibition factor
        - Leukocyte chemotaxis
        - Lymphoblast transformation
        - Immunofluorescence studies on intestinaly biopsy

IV. Verification of Cause-and-effect Relationship
   - Milk elimination-challenge test

(Cited from Bahna and Gandhi , 1983).

Physical examination:

Physical examination should include measurement of height and weight and head circumference. These values should be plotted on a growth grid. Child with significant malabsorption, his weight will be decreased compared with height and head circumference. The overall nutritional status is evaluated, skin turgor, amount of subcutaneous fat , evidence of muscle wasting,pretibial edema, and signs of dietary deficiency as well as evidence of acute or chronic disease. Evaluation of the allergic condition regarding severity and distribution should be recorded.

Laboratory Tests:

Initial laboratory tests will depend in large part on the patient's illness or problem. Tests such as complete blood count stool and urine analysis, quantitative immunoglobulins will be useful mostly in infants to evaluate the presence or absence of anemia and in ruling out chronic infection and or/ renal disease. A sweat test may be necessary to exclude cystic fibrosis. Esinophils found on examination of nasal mucous suggest an IgE-mediated allergy.

Immunologic tests:

IgE antibodies to food are associated with almost all immediate and some delayed food reactions. Serum IgE levels are often elevated in children with immediate- type food allergy, but may be low or normal. Quantitative measurement of serum IgA levels may be relevant because food allergies are somewhat more likely to develop in children with IgA deficiency(Bahna and Furukawa,1983).

1.**Skin testing:**

Skin testing with foods involves the application of dilute water-soluble suspensions of food extracts to the dermis. If the recipient has IgE antibody to the food antigen.,local wheal and flare-reactions typical of type I hypersensitivity are produced. Individuals may have positive skin tests in the absence of food allergy(false positive) (Metcalf,1984), allergic reactions to foods appear unusual in the face of negative skin tests(false negative)(Bock et al.,1978).

Skin testing with food extracts is performed by use of scratch or puncture techniques. Intradermal testing is avoided because of a greater danger of systemic reactions as well as local nonspecific irritant reactions.

Selected food extracts including nuts, egg, milk, soy and fish correlate reliably with allergic manifestations. Patients should never be advised that they are allergic to certain foods solely on basis of positive skin tests. It should be performed by a physician experienced in this procedure because of the risk of anaphylaxis.

Shash et al(1981) , concluded that for the evaluation of the intradermal skin tests as a diagnostic test of food allergy, it can be used but in addition to thorough history, elimination tests and challenge tests with the causative diet.

2-RAST and ELISA:

RAST(Radioallergosorbent test) and ELISA (Enzyme-linked immunosorbent assay) are directed at an in vitro demonstration of IgE directed to specific antigens. The RAST is the most commonly used diagnostic test, it is used where skin testing with extracts might pase a hazard, particularly of anaphylaxis, in patients suspected of being exquisitely sensitive to a particular antigen. It may be used in the evaluation of certain cases of eczema, where extensive skin lesions interfere with skin testing, in the evaluation of patients with dermographism. This test is generally less sensitive than the puncture(prick test).

Other disadvantage of RAST include cost, the availability of RASTs for only a limited number of foods, and the delay in obtaining results. The ELISA has similar potential to the RAST in the identification of food antigen-specific IgE,

3- Basophil histamine release:

Peripheral blood basophils from individuals with suspected food allergies can be examined in vitro to determine if they degranulate to dilute suspensions of food antigens. Degranulation requires the presence of IgE on the basophil specific to the suspected food (Sampson et al.,1987). It correlate with skin tests but do not establish a diagnosis of food allergy, are time consuming and appear to have no advantage over skin testing.

4-Controversial techniques:

Cytotoxic testing, provocative subcutaneous testing, and provocative sublingual testing use food extracts to diagnose food sensitivity. They involve subcutaneous injection or sublingual administration of sufficient antigen to elicit symptoms corresponding to patient's complaints (Metcalf,1984).

Elimination Diets:

When the relationship between ingestion of certain foods and resulting symptoms is unclear, the use of elimination diet may be warranted. The likelihood of establishing a diagnosis by use of elimination diets is higher when fewer foods are responsible for the symptoms.

The principle is that if the offending food is removed from the diet of the affected individual, the food induced illness will resolve. Elimination diets followed by return of suspected foods to the diet should be applied only in situations where symptoms are not life threatening, such as chronic hives or rhinitis.It is useful for the patient to remain on his usual diet ten to 14 days before any special diet is initiated. During that time, the patient should record the type and amount of foods ingested and the occurrence and character of adverse reactions (Sampson et al.,1987).

If no more than a few foods are suspected,the initial elimination diet can consist simply of removing these foods. Such an approach is more benefit in pediatrics where allergy to such foods as milk, egg, or soy is

common in early life. Care must be taken that suspected foods are not consumed while they are hidden in other foods.

Initiation of a severely limited diet is warranted if removal of one or several foods is not successful in eliminating symptoms or if multiple food sensitivities are suspected. It is used only for one to two weeks especially in children because more prolonged diet can lead to severe malnutrition.

Extensive elimination diets include the following: for infants younger than 3 months of age, milk substitute alone(casein hydrolysates such as Nutramigen or Pregestimil); for those 3-6 months, milk substitute and rice cereal, for those 6 months to 2 years, milk substitute with vitamin supplement,rice cereal, apple sauce,pears, carrots,squash, and lamb; for older children and adults, lamb and rice. Continuation of symptoms while following restricted diets indicates that symptoms are not due to foods or other avoided substances. If a relationship to diet is established, foods eliminated but not clearly implicated in causing symptoms should be returned to the diet individually at intervals of three to four days. If resumption of symptoms is associated with the introduction of specific foods, then this cause- and-effect relationship must be verified

by disappearance of symptoms on elimination of that food.

Although the procedure described may seem more applicable to outpatient evaluation, this procedure is unblinded and ,therefore,is subject to biased interpretation by the patient and the physician. Consequently, single or double- blind, placebo-controlled oral food challenge under direct medical supervision is necessary to diagnose food hypersensitivity accurately.

Controlled oral food challenge:

Food challenge may be performed in an " open", a " single blind ", or a " double blind " manner. In an open food challenge, both patient and physician are aware that a specific food is being administered. In a single-blind food challenge, only the patient is unaware of what food is being administered. In a double-blind food challenge, the patient remains unaware of whether a specific food or a placebo is being administered and a " neutral" observer such as a physician or nurse is also unaware of what is being administered. The results are scored by the patient and medical observer (Metcalf,1984).

Food challenge is most reliable when the resulting symptoms, such as erythema, urticaria, rhinitis, vomiting,

diarrhea, or asthma, can be observed directly in such a controlled situation. The amount of food administered as a test dose is ranging from 10 mg when the history suggests that small amounts of foods provoke symptoms to 8 gm when only large amounts foods lead to difficulty. Suspected foods may be administered by masking within other foods, by placement with opaque gelatin capsule, or by insertion via a nasogastric tube. A single gelatin capsule holds from 400 to 600 mg of dried food. Eleven grams of dried milk is equivalent to ½ cup in the liquid state. If 8 gm is tolerated, the food in its natural form and usual amounts can be administered to the patient.A single positive reaction such as hives or asthma to a food tested in a double-blind, placebo controlled food challenge may be taken as evidence of an adverse reaction to that food.

If placebo challenges are frequently positive, no association between the food and symptoms can be made. Acceptance of a positive test result does not prove that an immunologic mechanism is responsible. Adverse reactions may be due to conditions such as disaccharidase deficiency.

CHAPTER 12

DIFFERENTIAL DIAGNOSIS OF FOOD ALLERGY

DIFFERENTIAL DIAGNOSIS OF FOOD ALLERGY

Foods may be contaminated by a wide variety of substances that lead to reactions that may be confused with food allergy. The diagnostic process in food allergy starts with a careful medical history and physical examination directed at distinguishing food hypersensitivity from other causes of adverse reactions to foods. The yellow dye tartrazine, can cause non- IgE mediated hypersensitivity reactions in a small percentage of persons who may also be sensitive to aspirin(Stevenson et al.,1986).Table" 15 " illustrate differential diagnosis of food hypersensitivity (Metcalf,1984).

Several Gi tract diseases are associated with acute symptoms after food ingestion including hiatal hernia ,gastric and duodenal ulcers.Gastroeosophageal reflux may cause bronchial irritation, chronic cough , and wheezing in young children and infants.

In the newborn overfeeding and chalasia, which are estimated to occur to some degree in 50% of newborns, may result in vomiting after meals. Hiatal hernia,pyloric stenosis may present with recurrent vomiting after feeding.

Table "15" Differential diagnosis of food hypersensitivity

1. Additives and contaminants
   A. Dyes
      1. Tartrazine
   B. Flavorings and preservatives
      1. Nitrites and nitrates
      2. Monosodium glutamate
      3. Sulfiting agents
      4. Sodium benzoate
   C. Toxins
      1. Bacterial
         a. Botulism
         b. Staphylococcal intoxication
      2. Mushroom toxins
      3. Mycotoxins(aflatoxins)
      4. Seafood-associated
         a. Saxitoxin (shellfish)
         b. Scombroid poisoning(histamine)
         c. Ciguatera poisoning(fresh reef fishes as grouper,snapper)
   D. Infectious organisms
      1. Bacteria
         a. Salmonellosis
      2. Parasites
         a. Giardiasis
         b. Trichinosis
         c. Diphyllobothriasis
      3. Viruses
         a. Hepatitis
   E. Insect parts
   F. Mold antigens
   G. Accidental contaminants
      1. Heavy metals
      2. Pesticides
      3. Antibiotics
II. Gastrointestinal diseases
   A. Structural abnormalities
      1. Hiatal hernia
      2. Internal obstruction
   B. Enzyme deficiencies
      1. Lactase deficiency
      2. Glucose-6-phosphate dehydrogenase deficiency
      3. Galactosemia
   C. Malignancy
   D. Other
      1. Peptic ulcer disease
      2. Gallbladder disease
      3. Cystic fibrosis
III. Endogenous pharmacologic agents
   A. Caffeine
   B. Theobromine
   C. Histamine
   D. Tyramine
   E. Tryptamine
   F. Dopamine
   G. Norepinephrine
   H. Serotonin
   I. Phenylethylamine
   J. Alcohol
   K. Hallucinogenic alkaloids
IV. Psychological reactions
V. Other
   A. Collagen vascular diseases
   B. Endocrin disorders

(Cited from Metcalfe, 1984).

Hirschsprung's disease (congenital megacolon) often becomes apparent in the newborn period with diarrhea, vomiting, tachypnea, and irritability. A deficiency of lactase or other enzymes can resemble food allergy.

Lactase deficiency may be familial or acquired and can be associated with gastrointestinal infections and inflammatory bowel diseases. It may develop during infancy, childhood or adulthood. Lactase is the principal carbohydrate of milk, and individuals with lactase deficiency demonstrate milk intolerance.

Nausea, abdominal cramps, vomiting, diarrhea, facial flushing, headache, urticaria, and tingling sensation in the mouth result from the ingestion of large amounts of histamine produced by contaminating bacteria (especially proteus morgani and Klebsiella pneumonia (Merson et al., 1974).

Naturally occurring substances in some foods may cause problems confused with food allergy. Prunes, cucumbers, beans, fruits, soybeans, and onions contain substances that lead to gastroenteric symptoms by irritation

or pharmacologic activity. Amines such as tyramine and phenylethylamine, nitrates and nitrites, and alcohol may cause headaches. Methylxanthines (Caffeine, theobromine, and theophylline) are found in caffee, tea, cola and chocolate. These substances cause nervousness, tremor, and tachycardia in large amounts. Vasoactive amines (epinephrine, norepinephrine, tyramine, dopamine, histamine, and 5-hydroxytryptamine) are found in bananas, tomatoes, cheese, pineapples, and wines. Scombroid poisoning, due to the ingestion of tuna and related fish containing high levels of histamine, resembles food allergy and can be confirmed by finding high levels of histamine in the implicated fish.(Hughes and Merson,1976). Foods containing endogenous histamine are listed in Table(16).

Table " 16 " Foods Containing endogenous histamine

Food	Histamine (μg/gm)
Fermented cheeses(Swiss, cheddar.Gouda).	Up to 1330
Fermented drinks(wine)	30
Tinned foods	10-350
Dry pork and beef sausage	225
Spinach	37.5
Tomato	22
Other vegetables	Trace
Sardines	16
Anchovy fillets	44

(Cited from Sampson, 1986).

CHAPTER 13

MANAGEMENT OF FOOD ALLERGY

MANAGEMENT OF FOOD ALLERGY

The proper management of food allergy is identification of the food to which the patient is sensitive. In most instances, avoidance of the offending food is feasible and results in a satisfactory control of symptoms. Pharmacologic agents are often needed to inhance the symptomatic relief. In certain situations prophylactic medications may be worth considering. Patients who are highly sensitive to multiple foods, are often a challenge to treatment. In some food sensitive patients, additional factors may be involved and unless they are appropriately controlled, the management would be incomplete. An outline of the management of food allergies is presented as follows in table"17"(Bahna,1984).

1- Dietary treatment:

Dietary elimination is the most effective, safest and least expensive treatment of food allergy. Success depends on several factors ,Table" 18".In patients with severe symptoms, dietary elimination may need to be strict. The providing of a substitute is not needed except in two situation. First is the milk-sensitive infant, who should be provided with an appropriate formula such as soybean, casein hydrolysate, elemental diet, meat-base formula ,and

Table " 17 " Management of Food Allergies

Dietary
Avoidance of the offending food
Avoidance of cross-reacting foods
Rotation diets
Elimination diets
Pharmacologic
Symptomatic
Prophylactic
Antihistamines
Oral cromolyn
Ketotifen
Prostaglandin synthetase inhibitors
Hyposensitization
No proof of efficacy

(Cited from Bahna, 1984).

Table " 18 " Factors that Influence the Success of Dietary Elimination

Identification of all offending ingestants
Feasibility of their elimination from the diet
Their incorporation in various prepared foods
Completeness of food Labelling
Marketing under unfamiliar names
Degree of patient's compliance
Degree of patient's sensitivity
Nature of patient's symptoms
Concomitant involvement of non-ingestant allergens
Association with other factors, e.g.,G.I.disorders; Hormonal changes, emotions, exercise

(Cited from Bahna, 1984).

heat-treated cow milk. Second is the milk-sensitive pregnant or lactating woman should be provided with calcium and vitamin supplements(Bahna and Furukawa , 1983).

Milk-sensitive infants need to be provided with a milk substitute, which can be the only diet for infants up to six months of age, then they can be gradually supplemented with foods that do not contain cow milk. It might be prudent to delay the introduction of highly allergenic foods such as egg, chocolate, peanuts, citrus fruits and fish. Milk substitutes are usually not needed in older children or adults. Examples of these preparations are listed in Table " 19 "(Bahna and Gandhi,1983).

Food allergy in infants who are exclusively breast-fed requires elimination of the offending food from the mother's diet. Most food-sensitive infants and young children will tolerate the offending food after 1-2 years of avoidance (Bahna,1984).

Patients who are allergic to common food items (milk, egg, wheat, corn) that are often incorporated in many food preparations should be provided with special recipes free of that food. In this way the patient's

Table "19 " Common Commercial Cow's Milk Substitutes.

Substitute	Nature of Protein	Trade name & manufacturer
1. Soybean formula	Soy isolate	Isomil (Ross) Nursov (Wyeth) Pro-sobee(Mead-Johnson) i-Soyalac(Loma-Linda)
2- Protein hydrolysate	Enzymatically-digested bovine casein	Nutramigen(Mead-Johnson) Progestimil(Mead-Johnson)
3- Heat-treated cow's milk	Heat-altered cows' milk	Evaporated Milk (Carnation,Pet,National)
4- Elemental diet	Synthesized aminoacids	Vivonex(Norwich=Eaton)
5- Meat base formula	Beef heart	MBF Liquid(Gerber)
6- Goat's milk	Goat's milk	Evaporated Goat Milk(Meyenberg) Miracle(California Goat Dairy Assoc.)

(Cited from Bahna and Gandhi, 1983).

compliance can be enhanced. A wide variety of recipes for food allergic patients are available from several sources (Bahna and Furukawa,1983).

Some patients may have to avoid members of the same food family because of cross antigenicity. This is especially noticeable in certain food families such as citrus and fish (Bahna,1984). Whereas patients sensitive to cow milk generally tolerate beef, many of them do not tolerate goat's milk (Crawford and Grogan,1961).

Patients who have low to moderate degrees of sensitivity to multiple foods and can not follow an effective elimination diet may find a convenient dietary variation and a satisfactory control of symptoms on following a rotation diet. Members of the food family may be eaten on at a time on rotation basis. The quantity and frequency of intake are individually determined and depend mostly on patient's response(Bahna,1984).

There still remains a group of patients in whom the history is highly suggestive of food allergy but the causative food allergens are not identifiable. A trial of

one or more of the traditional " elimination diets " or hypoallergenic diets " may be worthwhile. In some patients, such diets may be therapeutic as well as diagnostic by reintroducing the eliminated foods one at a time at one to two week intervals and watching for recurrence of symptoms (Bahna and Furukawa,1983). Elemental diets(Vivonex) have been tried and showed promising results(Dockhorn and Smith, 1981). Because the prognosis of food allergy is usually excellent, particularly in young children, the patient may be cautiously challenged about every six to 12 months to avoid unnecessary prolonged deprivation or inconvenience (Bahna and Furukawa,1983).Table " 20 " shows examples of elemination diets(Truswell,1985).

Occasionally, food-related reactions occur only in the presence of certain factors, such as gastrointestinal disorders, hormonal changes, emotions, physical exercise, or other conditions(Bahna,1984).

Novey et al,1983, noted that postprandial exercise induced reactions may occur after the ingestion of either a specific food or any meal. Such factors should be identified and controlled.

Table " 20 " Examples of elimination diets

Elimination diets
The meat least likely to cause reactions is
Lamb
The least antigenic cereal is rice
Vegetables: peeled potatoes, carrots, and lettuce
Fruits: pears
Fat: a refined vegetable seed oil,eg. sunflower
Drink: Water and sugar.
Other foods are included in some elimination diets, depending on the type of reaction and the suspected ingredients.

(Cited from Truswell, 1984).

2) Pharmacologic treatment:

Symptomatic treatment:

Pharmacologic agents are often needed to control patient's symptoms, both at the time of presentation and whenever symptoms recur from exposure to the offending food. The choice of drugs depends on the type and severity of symptoms, whether an acute systemic reactions, urticaria, atopic dermatitis, rhinitis, bronchospasm, gastrointestinal disturbance or some other conditions. Therefore the drug of choice may be in the form of epinephrine, antihistamine, theophylline, inhaled or oral beta adrenergics, topical or systemic corticosteroids or a combination of these drugs.

Corticosteroid therapy is often needed to enhance the recovery of severe allergic gastroenteropathies of the protein- losing variety (Bahna and Furukawa,1983).

Prophylactic treatment:

In situations in which dietary elimination cannot be maintained at an optimal level, the additional intake of certain medications may prevent or minimize the development of symptoms.

The prophylactic medication may be taken on a regular basis or only before an anticipated exposure. It is not wise to permit frequent exposure to the food allergen under a contineous medication(Bahna,1984).

Antihistamines:

Histamine is the most common chemical mediator of hypersensitivity reactions to foods. Antihistamines compete with the histamine for its receptors. They are most effective when administered 20-60 minutes before exposure to the offending food. Ahti-H_1- receptor agents are available in various forms , inexpensive and easily administered. Their main disadvantage is sedation. A trial of more than one preparation, from different antihistamine groups,may be needed to select the optimal one for a particular patient (Bahna,1984). Occasionally, a combination of anti-H_1 and anti-H_2 agents gives better control than anti-H_1 alone(Plaut, 1979).

Cromolyn (disodium cromoglycate)oral preparations have shown promising results in the prophylaxis of food allergies (Businco et al.,1983). The drug is most effective when administered 30-60 minutes before ingestion of the food, and the effect lasts for a few hours. The optimal

dose usually in the range of 50-200 mg. Because it is not absorbed through the gastrointestinal mucosa, its action is mainly on the local mast cells. The drug has been used in patients of various ages, including infants, without significant side effects. Cromolyn powder used by inhalation for preventing asthma is contained in an insoluble form (Bahna,1984). Papageorgiou and others (1983) noted that the administration of oral cromolyn can prevent the elevation in neutrophil chemotactic activity in patients with milk-induced asthma.

Ketotifen in preventing symptoms of food allergy seem to be promising, particularly when the shocked organ is the skin or the gut(Neffen et al.,1980).

Unlike cromolyn,ketotifen is easily absorbed from the gastrointestinal tract and acts by inhibiting the release of histamine and slow- reacting substance of anaphylaxis (SRS-A) from mast cells, basophils, and neutrophils (Bahna,1984).

Prostaglandins seem to play a role in mediating certain food hypersensitivity reactions,particularly in the gastrointestinal tract. In these instances the levels of

PG-E2 and PG-F 2 α are increased in the plasma or in the secretion of the shock organ (Bahna and furukawa, 1983).

Buisseret and others (1978) showed that food induced reactions, mostly gastrointestinal, were prevented in five out of six patients by the intake of prostaglandin synthesis inhibitors (aspirin, indomethacin or ibruprofen) before challenge with the offending food. The effectiveness of these medications in any particular patient is unpredictable in the absence of determination of prostaglandin level, which requires a special assay that is not widely available (Bahna and Furukawa,1983).

3-Hyposensitization:

Unlike hyposensitization with pollen extracts for respiratory allergies, trial of hyposensitization with food extracts have not shown any convencing success, whether the route was subcutaneous, sublingual or oral(Golbert,1975).

The poor response to treatment with food extracts may be attributed to the presence of multiple immunologic mechanisms in food allergies, probably antigenic difference

between the treatment extract and the actual allergen and possibly many other factors. Certain modifications in the treatment extract or procedure may improve the response to food hyposensitization(Bahna,1984). In animal studies, immunologic tolerance can be induced through the oral route(Titus and Chiller,1981).

In man, successful oral desensitization has been reported for penicillin(Sullivan et al.,1982) and aspirin (Pleskow et al.,1982).

CHAPTER 14

PREVENTION OF FOOD ALLERGIES

PREVENTION OF FOOD ALLERGIES

Measures to reduce the incidence of food allergy are expected to be most rewarding when used in young children. Infants are considered at high risk for food allergy because of the increased intestinal mucosal permeability to incompletely digested macro-molecules and the lack of an adequate protection by secretory IgA at the mucosal membrane surface. The risk is especially high in potentially atopic infants(those from atopic families)(Bahna and Furukawa,1984).

The human fetus is capable of producing IgE by the 11 th week of gestation(Miller et al.,1973), there is evidence that intrauterine sensitization can occur by food antigens that cross the placenta from the maternal circulation(Kuroume et al.,1976). It would be prudent for preventive measures to begin during conception. The pregnant woman particularly in atopic families may be advised to avoid foods that she herself is allergic to and not to indulge in any particular food. She can limit even her milk intake to one or two glasses a day and take calcium and vitamin supplements (Bahna and Furakawa,1984).

The prediction of allergy in newborns is based upon several parameters which have been widely studied (Bousquet et al.,1984). Three parameters have been recognized as having a predictive capacity: cord serum IgE (Michel et al.,1980), genetic factors and sex of the newborn (Marsh et al.,1981).

Predictive value of cord blood and infant serum IgE for the development of allergy in infancy and childhood:

The examination of cord blood markers are of relevant importance in the determination of allergic risk in infancy. The best predictive capacity is obtained when both the family history of atopy and the titration of cord serum IgE are combined.(Bousquet et al.,1984). 52% to 82% of infants with elevated cord IgE levels compared with 5% to 30% with normal cord IgE levels subsequently developed obvious or probable allergies during early childhood (Zeiger et al.,1986). Table " 21 " demonstrate the predictive capacity of cord IgE and family history of atopy.

Kjellman and Croner(1984)performed a prospective follow-up studies of more than 1650 Scandinavian newborns for as long as 7 years. Defining elevated cord IgE levels

Table "21 ' Predictive Capacity of Cord Serum IgE and Parental Atopic Hisotry for the Subsequent Onset of Atopy

	Croner et al.	Businco et al.	Bousquet et al.	Dannaeus
Elevated IgE	70 %	61 %	52 %	50 %
Normal IgE	5 %	21 %	11 %	0 %
Atopic history	43 %		45 %	
No atopic history	12 %		16 %	
Elevated IgE + Atopic history	78 %		74 %	
Normal IgE + no atopic history	5 %		14 %	
Number of subjects	1701	102	322	53
Selection of subJects	none	atopic families	atopic families	

(Cited from Bousquet et, al, (1984).

as > 0.9 IU./ml, the sensitivity of predicting atopic disease by age 7 years approached 82%. However, the specificity of cord IgE levels were lower, since 30% of infants with normal cord IgE levels also developed atopy during childhood. Elevated cord IgE levels occurred in < 4% of children who had not developed atopy by the age 6 years. For predictive purposes,infants with more serious atopy represented by persistent symptoms at all three evaluation periods (18 months and 3 and 6 years) had elevated cord IgE levels in more than 94% of instances and were 100 times more likely to have high than low cord IgE levels. When cord blood IgE was less than 0.9 IU/ ml, atopy developed in 2%,19% and 30% of infants by 1.5 ,3 and 6 years of age, respectively. In comparison with the high-cord IgE group (> 0.9 IU/ml), 52%,69% and 82% of infants exhibited atopy at the same three age periods (1.5,3 and 6 years),respectively.

Croner and others(1982) showed that elevated cord blood IgE levels were also associated with high infant serum IgE and positive RAST tests at 18 months more often than were the low cord IgE levels, suggesting that both high and low IgE responders are already genetically coded at birth.

Elevated cord blood IgE concentrations combined with a positive immediate family history of atopy account for 67% of obvious allergic infants identified by 6 years. However, 33% of obvious allergic infants did not have either elevated cord IgE levels or an allergic family history and would not be identified at birth for being at risk for developing allergic disease in infancy or for institution of preventive measures (Kjellman and Croner, 1984).

Kjellman(1976) reported that in 207 selected healthy children born to nonatopic parents, 88% of initially high IgE levels remained elevated, 75% of infants (up to one year of age) with initial high IgE levels subsequently developed definite or probable atopic manifestations, in contrast to only 6% in infants with lower initial IgE levels. Moreover ,75% of children who subsequently developed definite and probable atopic disease were noted to have a high IgE level approximately 6 months before clinical manifestation of illness.

Recommendations for the prevention of food allergy:

An idealized strategy was formulated in an attempt to prevent, reduce, or delay the development of allergic

disease in at-risk newborns(Parental history of atopy or elevated cord IgE levels).The mainstay of this environmental engineering is the avoidance of highly allergenic foods (milk, eggs, soy, corn, wheat, peanuts, citrus and fish) during the first 12 to 36 months of life and aggressive avoidance of inhalant allergens throughout life. Breast feeding is strongly encouraged for long periods preferably for at least 6 months. Solid feeding is withheld until 6 months of age. Supplemental soybean and cow milk formulas are totally avoided during the first year because they contain potentially sensitizing proteins (Zeiger et al.,1986). Table " 22 " illustrate measures to prevent food allergy.

Nutramigen, an enzymatically prepared hydrolysate of casein which contains added corn oil, carbohydrates, minerals, and vitamins, has demonstrated hypoallergenic properties and nutritional adequacy. It possesses documented effectiveness in sensitized milk allergic or intolerant infants (Seban et al.,1977).

Breast fed infants may become allergic to food antigens ingested by the mother and excreted in her milk. When the offending food is identified and eliminated from the mother's diet the infant's symptoms disappear(Gerrard, 1979).

Table "22" Current Recommendations for the Prevention of Food Allergies in Populations at Risk

Strategy	Method
Identification of at risk individual or family	Documentation of IgE(atopic or other allergic reactivty individual or family members
Prevention of intrauterine Sensitization	Reduction of maternal allergenic load during last trimester by avoidance of allergenic foods
Prevention of postnatal sensitization to:	
Food antigens	Maternal avoidance
Transmitted through Breast milk	Diet during lactation and infant restrictive diet,elemental diet.
Other environmental antigens	Good educational programs on environmental control
Maximize immunologic competence	Encourage breast-feeding. immunotherapy when indicated to appropriate antigens
Pharmacologic agents	Antihistamines
	Inhibitors of prostaglandin synthesis (?)
	Disodium cromoglycate(cromolyn)

(Cited from Bellanti, (1984)

Lactating mothers tend to introduce solid food to the baby's diet at an age later than mothers of bottle fed infants(Sleigh and Ounsted,1975), a practice that contributes to the reduction or at least postpond the development of allergy (Saarinen, and Kajosaari,1980). Because gastrointestinal permeability is enhanced during diarrheal diseases it may be prudent to avoid introducing solid or highly allergenic food until complete recovery of the gastrointestinal mucosa (Bahna, and furukawa,1983).

Relatively " nonallergenic " solid foods such as noncorn, nonlegume vegetables, rice, meat,and noncitrus fruits are slowly added from 6 to 12 months of age. Milk is added after one year, followed shortly by corn,citrus, and nonpeanut legumes. Egg is introduced at 2 years and peanut and fish at 3 years (Zeiger et al.,1986). Another mainstay to the management of food allergy is the prevention of placental or breast milk passage of food antigens from the mother to the infant by avoiding of allergenic foods by the mother during the last trimester of pregnancy and during lactation.

Avoidance of milk, eggs, and peanut products and a reduction in wheat, soy, fish and citrus consumption

Lactating mothers tend to introduce solid food to the baby's diet at an age later than mothers of bottle fed infants(Sleigh and Ounsted,1975), a practice that contributes to the reduction or at least postpond the development of allergy (Saarinen, and Kajosaari,1980). Because gastrointestinal permeability is enhanced during diarrheal diseases it may be prudent to avoid introducing solid or highly allergenic food until complete recovery of the gastrointestinal mucosa (Bahna, and furukawa,1983).

Relatively " nonallergenic " solid foods such as noncorn, nonlegume vegetables, rice, meat,and noncitrus fruits are slowly added from 6 to 12 months of age. Milk is added after one year, followed shortly by corn,citrus, and nonpeanut legumes. Egg is introduced at 2 years and peanut and fish at 3 years (Zeiger et al.,1986). Another mainstay to the management of food allergy is the prevention of placental or breast milk passage of food antigens from the mother to the infant by avoiding of allergenic foods by the mother during the last trimester of pregnancy and during lactation.

Avoidance of milk, eggs, and peanut products and a reduction in wheat, soy, fish and citrus consumption

has been recommended (Bellanti,1984).

Supplemental calcium is taken(500 mg twice a day) in addition to prenatal vitamins while following this regimen. Major efforts must be directed at providing a suitable inhalant environment for the developing infant (Zeiger et al.,1986).

Infants are evaluated at 4 months, 1 year, and yearly thereafter by Multitest skin tests and serum IgE levels for the possible development of allergic sensitization. Early recognition of sensitization before the manifestation of illness could permit more aggressive manipulation of the infant's environment, which still permit prevention or delay of the allergic disease even after sensitization has occurred.

Diphthleria pertussis-tetanus immunizations are not given within 2 weeks of allergy skin testing to avoid the possibility of pertussis- induced relative B-adrenergic blockade and increased potential for allergic sensitization (Zeiger et al.,1986).

Most older children, with slow reactions such as migraine to many foods will require an oligoantigenic diet

(Egger et al.,1983). Avoidance of certain categories of foods may sometimes be useful, e.g. for intolerance (the evidence that it is allergy is not clear, but it probably is) to a range of food additives in factory-produced foods, especially colours (e.g.tartrazine) and preservatives (e.g. benzoates). It is easy to prevent food allergy which comes on quickly to a single unusual food (e.g. urticaria induced by Shellfish), by avoidance of the antigen to which the patient is sensitized. Other symptoms (e.g. eczema or migraine) come on more slowly and may be provoked by several foods in the same child. Prevention is difficult, but recent double-blind controlled trials have confirmed the phenomenon (Soothill,1984). For some, avoidance of known common antigens, e.g. milk, eggs, chicken and beef (in eczema), may be effective (Atherton et al.,1978).

Use of pharmacologic agents in the prevention of food allergy:

The use of pharmacologic agents may be useful in the management of food allergy either for treatment or prophylaxis. In the case of prophylaxis when strict avoidance of the offending food can not be attained, symptoms may be prevented or minimized by the use of certain drugs. The drug to be chosen, its dosage and frequency should be individualized depending on the age of the patient, the frequency of the

exposure, the particular shock organ, the severity of symptoms and the pathogenic mechanism involved. Since the latter is, difficult to determine in clinical practice, these medications are empirically used.

The use of antihistamines has been tried with varying results in food allergy. H_1, receptor antihistamines alone or in certain patients in combination with H_2 receptor antagonists may be given 20-60 minutes before the anticipated exposure to the offending food.(Bellanti,1984).

Oral disodium cromoglycate (cromolyn) has been used in several studies and has shown favourable results in the prevention of symptoms of food hypersensitivity in a dose of 30 mg/kg b.w/day, (Kacoshis and Gryboski,1979 and Businco et al.,1983).

Inhibitors of prostaglandin synthesis have been used in the treatment with mixed results. The reactions were prevented in five out of six patients by the intake of prostaglandin synthesis inhibitors. At the present time, the use of these drugs remains investigational. (Bellanti,1984).

New approaches to the prevention of food allergy:

The prevention of IgE mediated disorders could be approached by intervention at the level of immune regulation of IgE production. Possibilities include the administration of suppressor factors of allergy at critical times during development.(Bellanti,1984).

Oral desensitization to inhalant and food allergens or selective employment of a series of drugs (cromolyn-like derivatives), The use of IgE - derived peptides to block atopic reactions, has been suggested by Hamburger and his co-workers,1983. The development of immunologic tolerance to various food antigens is yet another approach which has been successfully demonstrated in the experimental animal(Katz,1980).

The physician is left at present with modification of the environment by reducing the allergenic load or by the various strategies described previously.(Bellanti, 1984).

CHAPTER 15

SUMMARY AND CONCLUSION

SUMMARY AND CONCLUSION

Allergic disease, which usually appears in childhood and is one of the most common reasons for pediatric visits, can become a lifelong problem. Allergy is one of the most common causes of acute and chronic diseases in children. Over 20% of the pediatric population is allergic .

Food allergy is widely perceived by the public as a major health problem, its incidence among children has been variously estimated from 0.3 % to 7.5% and the incidence decreases with age.

Food allergy is defined as an immunologic reaction resulting from the ingestion of a food or food additives.

A number of well designed studies have suggested that food allergy plays a significant role in the pathogenesis of many diseases: urticaria, eczema, cow's milk protein enteropathy, infantile colitis, colic, migraine, and hyperactivity. While asthma and inflammatory bowel disease may sometimes be associated with food allergic reactions.

Prospective clinical studies of infants born to parents with atopy had shown that the risk for allergy approaches 50% to 58% in unilateral allergic parentage, and 67% to 100% with bilateral allergic parentage.

The majority of allergic reactions to foods are IgE mediated, mast cell-dependent and immediate hypersensitivity reactions.

Breast feeding decreases allergic sensitization by reducing both exposure to and intestinal absorption of food antigens. The protective role of human breast milk immunoglobulins, especially sIgE, in inhibiting absorption of antigenic substances has been documented in human neonates.

All food proteins taken orally, are likely to be allergenic to a some degree. In infancy and early childhood, proteins in cow milk and soy are the major cause of food allergy.

Wheat protein, egg protein,rice, fish, chicken meat, and corn as well as tomatoes, oranges, bananas and chocolates have been reported to produce gastrointestinal

symptoms in some individuals.

Food allergy is associated in some cases with behavioral variations, the most common of which are allergic tension fatigue syndrome, hyperactivity with poor attention span, and migraine.

Diagnosis of food allergy starts with a careful history. Skin tests and radioallergosorbent test are helpfull.

Confirmation can only be attained by double-blind or single-blind, placebo-controlled oral challenge with the suspected foods. These tests are performed to distinguish food allergy from other causes of adverse reactions to foods.

The proper management of food allergy is by identification of the food to which the patient is sensitive. Avoidance of the offending food, in most instances, will result in a satisfactory control of symptoms .

Pharmacologic agents are often needed to inhance the symptomatic relief. In certain situations,prophylactic

medications may be worth considering. Measures to reduce the incidence of food allergy are expected to be most rewarding when used in young children.

CHAPTER 16

RECOMMENDATIONS

RECOMMENDATIONS

For proper prevention of food allergy in infants and children, general considerations should be put in mind:

- Infants are considered at high risk for developing food allergy because of the increased intestinal mucosal permeability to incompletely digested macromolecules and the lack of an adequate protection of $sIgA$ at the mucosal membrane surface.

- The risk is especially high in potentially atopic infants (those from atopic families).
- The human fetus is capable of producing IgE by 11 weeks of gestation, there is an evidence that intrauterine sensitization can occur by food antigens crossing placenta from the maternal circulation.
- Preventive measures for food allergy should begin during conception.

  The pregnant woman of atopic families should avoid foods that she herself is allergic to. She can limit her milk intake to one or two glasses a day.
- Early detection of food allergy in newborn, by measuring serum IgE, is helpful for proper management.

Recommendations for the prevention of food allergy in at risk, newborns:

- Avoidance of highly allergenic foods(milk, egg, soy, corn, wheat, peanuts, nuts, citrus and fish) specially during the first 12 to 36 months of life and aggressive avoidance of inhalant allergens throughout life.
- Breast feeding is strongly encouraged for long periods, preferably for at least 6 months because breast feeding (in particular colostrum) promotes functional maturation of the intestine and limits macromolecular absorption by providing IgA to the infant. Prolonged breast feeding reduce allergic sensitization and reduce eczema in children during 1 st three years of life.
- Solid feeding is delayed until 6 months of age because solid foods contain potentially sensitizing proteins.
- Supplemental soybean and cow's milk formula are totally avoided during the first year

  Some investigators incriminate cow's milk as a cause of sudden infant death syndrome.
- Nutramigen, an enzymatically prepared hydrolysate has demonstrated hypoallergenic properties and nutritional adequacy.

- Elimination of the allergenic food from the mother's diet during breast feeding.
- Avoid introduction of solid or highly allergenic foods during diarrheal diseases in infants, and children.
- Relative nonallergenic solid foods and non citrus fruits are gradually added from 6 to 12 months of age. Milk is added after one year, followed by corn,citrus and non peanut legumes, egg is introduced at 2 years and peanut and fish at 3 years.

- Mother should avoid food antigens during the last trimester of pregnancy and during lactation to prevent passage of these food antigens through placenta or breast milk.
- Supplemental calcium (500 mg twice daily) with prenatal vitamins while following this regimen.
- Infants are evaluated at 4 months, 1 year and yearly thereafter. Early recognition of sensitization before the manifestation of illness could permit aggressive manipulation of infant's environment.
- Avoid giving D.P.T. vaccination within 2 weeks of allergy skin testing.
- Use of hypoallergenic diet for children suffering from migraine due to food.

- Treatment of hyperkinesis can be established by psychotherapy and salicylates-free diet.

- The use of certain drugs for prophylaxis if strict avoidance of the offending food is not attained.
- New approaches for the prevention of food allergy is not practical till now and need further investigations.

LIST OF ABBREVIATIONS

C 3a	Complement No.3 a(anaphylatoxins)
C 5a	Complement No.5 a(")
CIE	Crossed immunoelectrophoresis
CMPA	Cow's milk protein allergy
CRIE	Crossed radio-immunoelectrophoresis
ELISA	Enzyme-linked immunosorbent assay
F.A.	Food Allergy
GIT	Gastrointestinal tract
HLA	Human leucocytic antigen
sIgA	Secretory immunoglobulin A
IgE	Immunoglobulin E
IgG	Immunoglobulin G
IgM	Immunoglobulin M
PGE	Prostaglandin E
PGF alpha 2	Prostaglandin F alpha
SCG	Sodium cromoglycate
SRS-A	Slow reacting substance of anaphylaxis
RAST	Radioallergosorbent test.

REFERENCES

REFERENCES

Aas,K.(1978):
"The diagnosis of hypersensitivity to ingested foods."
Clin. Allergy 8:39.

Allansmith, M., and Buell,D.N.(1964):
" The relationship of gamma-IA globulin and reagin in cord sera ".
J. Allergy 35: 339.

Allen,D.H. and Baker,G.J.(1981):
" Chinese-restaurant asthma ".
N.Engl. J. Med. 305:1154.

Ament,M.E. and Rubin,C.E.(1972):
" Soy protein-another cause of the flat intestinal lesion".
Gastroenterology 62:227.

Anderson,K.J.;Mclaughlan,P.,Devey,M.E. and Coombs, R.R.A.(1979):
" Anaphylactic sensitivity of guina pigs drinking different preparations of Cow's milk and infant formulae".
clin. Exp. Immunol. 35:454.

Asperen,V.P.P., and Mellis,C.M.(1983):
" Immediate food hypersensitivity reactions on the first known exposure to the food".
Arch. Dis. Child 58:253.

Atherton,D.J.(1980):
" Dietary antigen avoidance in the treatment of atopic dermatitis".
Acta. Derm. Venereol. 92:99.

Atherton, D.J.(1984):
" Diagnosis and management of skin disorders caused by food allergy ".
Ann. Allergy. 53:623.

Atherton,D.J.; sewell,M.; Soothill,J.F.; Wells,R.S. and Chilvers, C.E.D.(1978):
"A double blind controlled crossover trial of an antigen avoidance diet in atopic eczema".
Lancet. 1:401.

Bahna,S.L.(1984):
"Management of food allergies ".
Ann. Allergy 53: 678.

Bahna,S.L. and Furukawa,C.T.(1983):
" Food allergy: diagnosis and treatment".
Ann. Allergy 51: 574.

Bahna,S.L. and Gandhi,M.D.(1983):
" Milk hypersensitivity: Practical aspects of diagnosis, treatment and prevention".
Ann. Allergy 50: 295.

Baker,G.J., Collett,P., and Allen,D.H.(1981):
" Bronchospasm induced by metabisulfite containing foods and drugs ".
Med. J. Aust.,2: 614.

Barnett,D.Bonham, B. and Howden,M.E.H .(1987):
" Allergenic cross-reactions among legume foods. An in vitro study ".
J. Allergy Clin. Immunol 79 :433.

Barret, J.T., In " Textbook of Immunology"(1983):
"An introduction to immunochemistry and immuno-therapy", Edited by Barret J.T,4 th edition, P.375.
The C.V. Mosby Company, St. Louis.

Bazaral M., Orgel ,H.A.& Hamburger R.N.(1974):
" Genetics of IgE and allergy: serum IgE levels in twins".
J. Allergy Clin. Immunol.54:288.

Bellanti,J.A.(1984):
" Prevention of food allergies".
Ann. Allergy 53: 683.

Bernstein,I.D. and Ovary,Z.(1968):
" Absorption of antigens from the gastro-intestinal tract".
Int. Arch. Allergy Appl. Immunol 33:521.

Blands,J.,Diamant,B.,Kallas,P., Deffner,K.L., and Lowenstein,H .(1976):
"Flour allergy in bakers: identification of allergenic fractions in flour and comparison of diagnostic methods".
Int. Arch. Allergy Appl. Immunol.52:392.

Bock,S.A.(1986):
" A critical evaluation of clinical trials in adverse reactions to foods in children".
J. Allergy Clin. Immunol.78:165.

Bock, S.A.,Lee,Y.,Remigio,L.K. and May,C.D.(1978):
"Studies of hypersensitivity reactions to foods in infants and children ".
J. Allergy Clin. Immunol.62: 327.

Bousquet,J., Menardo,J.L. and Michel,F.B.(1984):
" Predictive capacity of cord blood IgE for the development of allergy in infancy and childhood".
Ann. Allergy 53: 692.

Brown, E.B., Jasephson,B.M., Levine,H.S. and Rosen,M.(1969):
" A prospective study of allergy in a pediatric population".
Am.J. Dis. Child. 11 :693.

Buckley,R.H. and Metcalf,D.(1982):
" Food Allergy ".
JAMA 248:2627.

Buisseret, P.D ., Youlten,L.J.F., Heinzelmann,D.I., and Lessof,M.H.(1978):
" Prostaglandin-synthesis inhibitors in prophylaxis of food intolerance".
Lancet 1:906.

Businco,L.,Benincori, N. , and Cantani,A.(1984):
" Epidemiology, incidence and clinical aspects of food allergy ".
Ann. Allergy 53 :615.

Businco,L.,Cantini,A.,Benincori, N .,Perlini,R.,Infussi, R., De-Angelis,M. and Businco,E.(1983):
"Effectiveness of oral sodium cromoglycate in preventing food allergy in children".
Ann. Allergy 51:47.

Carrillo,D.T.,Agust,C.M. and Giori,M.I.(1986):
" Detection of IgE specific for egg yolk by enzyme immuno-assay: description of a case".
Allergol. Immunopath. 14:9.

Chandra,R.K.(1979):
" Prospective studies of the effect of breast feeding on incidence of infection and allergy".
Acta Pediatr. Scand.68:691.

Chetty,A.(1982):
"Extrinsic allergic alveolitis due to milk allergy: Case report and review of the literature".
Ann. Allergy 48:113.

Coombs,R.R. A., and Mc Laughlan,P.(1984):
" Allergenicity of food proteins and its possible modification ".
Ann. Allergy 53:592.

Crawford ,L.V. and Grogan,F.T.(1961):
" Allergenicity of cow's milk proteins: Relationship to goat's milk proteins as studied by serum, agar precipitation".
J. Pediatr. 59:347.

Crayton,J.W.(1986):
" Adverse reactions to foods: relevance to psychiatric disorders ".
J. Allergy Clin. Immunol 78:243.

Croner,S.,Kjellman,N.I., ERiksson,B., Roth,A.(1982):
" IgE screening in 1701 newborn infants and the development of atopic disease during infancy ".
Arch. Dis. Child. 57:364.

Dannaeus,A., and Johansson, S.G.O.(1979):
" A follow-up of infants with adverse reactions to cow's milk.
Acta Pediatr. Scand.68:377.

Dannaeus,A.,Johansson,S.G.O.,Foucard,T., Ohman,S.(1977):
" Clinical and immunological aspects of food allergy in childhood. I. Estimation of IgG, IgA, and IgE antibodies to food antigens in children with food allergy and atopic dermatitis".
Acta. Pediatr. Scand. 66:31.

Dockhorn, R.J. and Smith, T.C.(1981):
"Use of a chemically defined hypoallergenic diet (Vivonex) in the management of patients with suspected food allergy intolerance ".
Ann. Allergy 47: 264.

Dohan,F.C.,Harper,E.H.,Clark,M.H., Bodrigue,R.B. and Zigas,V.(1984):
"Is schizophrenia rare if grain is rare?
Biol. Psychiatry 19:385.

Dolby,A.E., and Walker,D.M.A.(1975):
" Trial of cromoglycic acid in recurrent aphthous ulceration".
Br.J. of Oral Surgery 12: 292.

Donnally,H.M.(1930):
" The question of elimination of foreign protein (egg white) in woman's milk".
J. Immunol. 19:15.

Dumont,G.C.L.,Beach,R.C., Menzies,I.S.(1984):
" Gastrointestinal permeability in food-allergic eczematous children".
Clin.Allergy 14:55.

Eastham,E.J.,Lichiauco,T., and Grady, M.I.(1978):
" Antigenicity of infant formulas: role of immature intestine on protein permeability".
J.Pediatr. 93:561..

Egger,J.,Carter,C.M.,Graham, P.J., Gumley,D. and Soothill,J.F.(1985):
" Controlled trial of oligoantigenic treatment in the hyperkinetic syndrome".
Lancet.1:540.

Egger,J.,Carter,C.M.,Wilson,J., Turner,M.W. and Soothill,J.F.(1983):
" Is migraine food allergy ? A double-blind Controlled trial of oligoantigenic diet treatment".
Lancet 2:865.

Feingold,B.F.(1975):
"Hyperkinesis and learning disabilities linked to artificial food flavors and colors"
Am.J. Nurs. 75:797.

Fergusson,D.M.,Horwood,L.J.,Beautrias,A.L.(1981):
" Eczema and infant diet".
Clin. Allergy 11:325.

Fergusson,D.M.,,Horwood,L.J.,Shannon,F.T.(1983):
" Asthma and infant diet ".
Arch. Dis. Child 58: 48.

Finkelestein,H.(1905):
Kuhmilch als Ursache akuter ernahrungstorungen bei Sauglingen. Monatsschr Kinderheilk 4:65.
Quoted from Smith,J.A.W.,Ford,R.P.K. and Phillips,A.D. (1984): The spectrum of gastrointestinal allergies to food.
Ann.Allergy 53:629.

Ford,R.P.K., and Taylor,B.(1982):
" Natural history of egg hypersensitivity in childhood".
Arch. Dis. Child.57: 649.

Foreget,P.,Eggermont,E.,Morchall,G., Jasken,J., Melchovic,S.(1978):
"Eosinophilic infiltration of the oesophagus in the infant ".
Acta. Pediatr. Belg. 3191.

Frick,O.L.,German,D.F.,Mills,J.(1979):
" Development of allergy in children.
1. Association with virus infections".
J. Allergy Clin. Immunol. 63:228.

Frier,S.,Kletter,B., Grey,I., Lebenthal,E. and Geifman,M, Lebenthal, E., and Geifman,M.(1969):
" Intolerance to milk protein".
J. Pediatr. 75:623.

Galen(130-219 A.D.) Quoted from Wood C.B.S.(1986):
"How common is food Allergy ?"
Acta Pediatr. Scand.323:76.

Gerrard,J.W.(1979):
"Allergy in breast fed babies to ingredients in breast milk".
Ann. Allergy 42:69.

Gerrard,J.W., Horne,S.,Vickers,P.,MacKenzie,J.W.A., Goluboff,N. Garson. J.Z. and Maningas,C.S.(1974):
" Serum IgE levels in parents and children".
J, Pediatr. 85:660.

Gjesing,B. and Lowenstein, H.(1984):
" Immunochemistry of food antigens".
Ann. Allergy 53: 602.

Golbert,T.M. (1975):
" A review of controversial diagnostic and therapeutic techniques employed in allergy".
J. Allergy Clin. Immunol. 56: 170.

Goldman,A.S., anderson,D.W.,Sellers, Saperstein,S., Kinker,W.T., and Happern,S.R.(1963): " Milk allergy". Pediatrics 32: 425.

Goldstein,G.B., and Heiner,D.H.(1970): " Clinical and immunological perspectives in food sensitivity". J. Allergy 46: 270.

Grant,E.C.G.(1979): " Food allergies and Migraine". Lancet 1;966.

Graysowski,E.A.,Barile,M.F.,Lee,W.B., and Stanley,H.R.(1966): " Recurrent aphthous stomatitis clinical, therapeutic, histopathologic, and hypersensitivity aspects". J.A.M.A.196:637.

Gryboski, D.j.(1967): "Gastrointestinal milk allergy in infants." Pediatrics 44:354.

Gunther,M.,Check,E.,Motthems,R.H. and Coombs,R.R.A.(1962): " Immune responses in infants to cow's milk proteins taken by mouth". Int. Arch. Allergy Appl, Immunol. 21:257.

Hamburger F.(1901): Biologisehas uber die Eiweisskorper der Kuhmilch und uber Sauglingsnahrung. Wein Klin Wochenschr 14:1202. Quoted from Businco,L.,Benincori, N, and Cantani,A.(1984):Epidemiology,incidence and clinical aspects of food allergy. Ann. Allergy 53: 615.

Hamburger,R.N., Heller,S.,Mellan,M.H.,Conner,R.D. and Zeyer,R.S.(1983): " Current status of the clinical and immunologic consequences of a prototype allergic disease prevention program". Ann.Allergy 51:281.

Hammar, H. (1977): " Provocation with cow's milk and cereals in atopic dermatitis ". Acta. Derm. Venereol 57:159.

Hanington,E.(1971):
" Migraine".
Trans. Med. Soc.87:32.

Hannuksela,M.(1983):
" Food allergy and skin diseases ".
Ann. Allergy,51:269.

Hannuksela, M. and Lahti,A.(1977):
" Immediate reactions to fruits and vegetables".
Contact. Dermatitis. 3:79.

Harley,J.P.,Matthews,C.G., and Eichmann,P.(1978):
" Synthetic food colors and hyperactivity in children: a double blind experiment".
Pediatr. 62:975.

Hein,E.W., and Kishore,R.(1984):
" Allergic disease in children".
Postgraduate Medicine 75:169.

Heiner,D.C.(1983):
" Food allergy and respiratory disease".
Ann. Allergy 51:273.

Heiner,D.C.(1984):
" Respiratory diseases and food allergy".
Ann. Allergy 53:657.

Heird,W.D. and Hansen,I.H.(1977):
" Effects of colostrum on growth of intestinal mucosa".
Pediatr. Res.11:406.

Hemmings,W.A. and Kulangara, A.C.(1978):
" Dietary antigens in breast milk".
Lancet 2: 575.

Hill,D.J.,Davidson,G.P.,Cameron,D.J.S. and Barnes,G.L.(1979):
" The spectrum of cow's milk allergy in childhood".
Acta.Pediatr. Scand.68:847.

Hill,D.J.,Firer,M.A.,Shelton,M.J. and Hasking.C.S.(1986):
" Manifestation of milk allergy in infancy.
Clinical and immunological findings".
J, Pediatr. 109:270.

Hippocrates (570-460 B.C.). Quoted from Wood C.B.S.(1986):
How common is food allergy?
Acta Pediatr. Scand, 323:76.

Hoffman,D.R.(1975):
" The specificities of human IgE antibodies
combining with cereal grains".
Immunochem. 12:535.

Hoffman,D.R., Day,E.A., and Miller,J.S.(1979):
" The major heat-stable allergen of
shrimp".
Fed.Proc.38:1415.

Hoffman,D.R.,Day,E.D. and Miller J.S.(1981):
" The major heat stable allergen of shrimp".
Ann. Allergy 47:17.

Hughes,E.C.(1978):
" Use of chemically defined diet in the diagnosis
of food sensitivities and the determination of
offending foods".
Ann.Allergy 40:393.

Hughes,J.M., and Merson,M.H.(1976):

"Fish and shellfish poisoning".
N, Engl.J.Med.295:1117.

Jansson,B.,Kristjansson,E.,Nilsson,L.(1984):
" Schizophrenic psychotic picture decreased
in a patient given gluten-free diet".
Lakartidningen 81:448.

Jarrett,E.E., and Hall,E.(1979):
" Selective suppression of IgE antibody responsi-
veness by maternal influence".
Nature 280:145.

Jenkins,H.R., Milla,P.J., Pincott,R.R., Soothill,J.F. and Harries,J.T.(1983):
" Food allergy: the major cause of infantile colitis".
Pediatr.Res.(Abstract) 431.

Johnston ,D.E. and Dutton,A.M.(1966):
" Dietary prophylaxis of allergic diseases in children".
N.Engl.J. Med.274:715.

Juhlin,L.(1980):
" Incidence of intolerance to food additives".
Int.J. Dermatol.19:548.

Juhlin,L.(1981):
Recurrent urticaria:" Clinical investigation of 330 patients".
Br.J. Dermatol.104:369.

Juto,P.,Engberg,S., and Winberg,J.(1978):
" Treatment of infantile atopic eczema with a strict elimination diet".
Clin. Allergy 8: 493.

Juto,P., Moller,C.,Engberg,S., Bjorksten,B.(1982):
" Influence of type of feeding on lymphocyte function and development of infantile allergy".
Clin.Allergy 12:409.

Kacoshis,S., and Grybaski,J.D.(1979):
" Use of cromolyn in combined gastrointestinal allergy".
J. Ann.Med. Assn.242:1169.

Kajosaari,M., and Soarinen,U.M.(1983):
" Prophylaxis of atopic disease by six months total solid food elimination".
Acta. Pediatr. Scand.72:411.

Kaplan,M.S. and Solli, N.J.(1979):
" Immunoglobulin E to cow's milk protein in breast fed atopic children".
J. Allergy Clin. Immunol 64:122.

Katz,D.H.(1980):
"Recent studies on the regulation of IgE antibody synthesis in experimental animals and man".
Immunology 41, 1.

Katz,A.J.,Goldman, H. and Grand,R.J.(1977):
" Gastric mucosal biopsy in eosinophilic (allergic) gastroenteritis".
Gastroenterology 73:705.

Kilshaw , P.J., Heppell,L.M.J. and Ford,J.E.(1982):
" Effects of heat-treatment of cow's milk and whey on the nutritional quality and antigenic properties".
Arch.Dis.Child.57:842.

Kittler,F.J. and Baldwin,D.G.(1970):
" The role of allergic factors in the child with minimal brain dysfunction".
Ann. Allergy 28:203.

Kjellman,N,I.M.(1976):
" Predictive value of high IgE levels in children".
Acta. Pediatr. Scand. 65:465.

Kjellman,N.I.M(1981):
" Effect of parental smoking on IgE levels in children".
Lancet 1:993.

Kjellman,N.M, and Croner,S.(1984):
" Cord blood IgE determination for allergy prediction- a follow-up to seven years of age in 1651 children".
Ann. Allergy 53:167.

Kjellman,N,I.M., and Johansson,S.G.O(1979):
" Soy versus cow's milk in infants with a biparental history of atopic disease: development of atopic disease and immunoglobulins from birth to 4 years of age ".
Clin.Allergy 9:347.

Kriebel,C.W.; Kraft,S.C., and Rothberg,R.M.(1969):
" Locally produced antibodies in human gastrointestinal secretions".
J. Immunol.103:1268.

Kuroume,T.,Oguri,M.,Matsumura, T., Iwasaki,I., Kanbe,Y., Yamada,T.,Kawobe,S., and Negishi,K.(1976):
" Milk sensitivity and soybean sensitivity in the production of eczematous manifestations in breast-fed infants with particular reference to intrauterine sensitization".
Ann.Allergy 37:41.

Kushimato, H., and Aoki,T.(1986):
" Masked type I wheat allergy: Relation to exercise induced anaphylaxis".
Arch. Dermatol.121:355.

Langeland,T.(1982a):
" A clinical and immunological study of allergy to hen's egg white: Antigens in hen's egg white studied by crossed immunoelectrophoresis(CIE)".
Allergy 37:323.

Langeland T.(1982b):
" A clinical and immunological study of allergy to hen's egg white: Allergens in hen's egg white studied by crossed radio-immunoelectrophoresis (CRIE)".
Allergy 37:521.

Langeland,T., and Harbitz,O.(1983):
" A clinical and immunological study of allergy to hen's egg white: Purification and identification of major allergen(Antigen 22) in hen's egg white".
Allergy 38:131.

Lemanske,R.F,Atkins, F.M. and Metcalf,D.D.(1983):
" Gastrointestinal mast cells in health and disease".
J. Pediatr. 103:177.

Lucretius Caro T. (1st Century B.,C.):
De Rerum Natura ,IV,637. Quoted from Businco,L., Benincori, N. and Cantani,A.(1984):" Epidemiology, incidence and clinical aspects of food allergy".
Ann.Allergy 53:615.

Lyngkoran , N.,Abidain,Z.,Meng,L.L. and Yadav,M.(1982):
"Egg-protein-induced villous atrophy".
J.Pediatr.Gastroenterol.Nutr. 1:29.

Malish,D.,Glovsky,M.M.,Hoffman,D.R., Ghekiere,L. and
Hawkins,J.M.(1981):
"Anaphylaxis after sesame seed ingestion".
J.Allergy Clin. Immunol.67:35.

Marsh,D.G.,Bias, W.B.,Ishizaka,K.(1974):
" Genetic control of basal serum IgE level
and its effect on specific reaginic sensitivity".
Proc. Natl .Acad.Sci.USA 71:3588.

Marsh,D.G.,Meyers,D.A. and Bias,W.(1981):
"The epidemiology and genetics of atopic
allergy".
N.Engl.J.Med.305:1551.

Mattews,D.M.(1974):
" Absorption of amino-acids and peptides from
the intestine".
Clin.Endocrinol. Metab.3:3.

May,C.B., and Alberto,R.(1972):
" In vitro responses of leukocytes to food proteins
in allergic and normal children: lymphocyte
stimulation and histamine release".
Clin.Allergy 2:335.

May,C.D.(1984):
"Food sensitivity: facts and fancies".
Nutr.Rev. 42:72.

Mc Laren,D.S.(1981):
" Nutrition and its disorders" editor, third
edition, p.231. Churchill Livingstone. Edinburgh.

Mc Laughlan,P.,Anderson,K.J. and Coombs, R.R.A.(1981a):
" An oral screening procedure to determine the
sensitizing capacity of infant feeding formulae".
Clin.Allergy 11:311.

Mc Laughlan,P.,Anderson,K.J.,Widdowson,E.M. and Coombs,R.R.A.(1981b):
" Effect of heat on anaphylactic-sensitizing capacity of cow's milk, goat's milk and various infant feeding formulae fed to guina pigs".
Arch. dis.Child. 56: 165.

Mc Laughlan,P., and Coombs ,R.R.A(1983):
" Latent anaphylactic sensitivity of infants to cow's milk proteins: histamine release from blood basophils".
Clin.Allergy 13:1.

Mellon,M.,Heller,S. Conner,R.D., Hamburger,R.N., and Zeiger, R.S.(1983):
"No increase in cow's milk (C.M.) sensitization after delayed CM ingestion in infancy".
J.Allergy Clin. Immunol 71:40.

Merson,M.H., Baine,W.B.,Gangerosa,E.J., and Swanson, R.C.(1974):
" Scombroid fish poisoning".
J.A.M.A.228:1268.

Metcalf,D.D.(1984):
"Food hypersensitivity".
J. Allergy Clin. Immunol 73:749.

Metcalf,D.D.(1985):
"Food allergens".
Clin.Rev. Allergy.3:331.

Michel,F.B.,Bousquet,J.,Greillier,P., Coulomb,Y. and Robinet-Levy,M.(1980):
" Comparison of cord blood IgE concentrations and maternal allergy for the prediction of atopic disease in infancy".
J. Allergy Clin. Immunol 65:422.

Miller,D.L.,Hirvonen ,T., and Giltin,D.(1973):
" Synthesis of IgE by the human conceptus".
J.Allergy Clin. Immunol 52:182.

Millman,M.; Campbell, M.B.; Wright ,K. and Johnston,A.(1976):
" Allergy and learning disabilities in children".
Ann. Allergy 36:149.

Molkhou,P., and Waguet ,J.C.(1981):
" Food allergy and atopic dermatitis in children:
Treatment with oral sodium cromoglycate".
Ann. Allergy 47:173.

Monro,J.,Brostoff,J., Carini,C. and Zilkha,A.(1980):
"Food allergy in migraine: a study of dietary
exclusion and RAST".
Lancet 2:1.

Monro,J.,Carini,C., and Brostoff,J.(1984):
"Migraine is a food allergic disease".
Lancet 2:719.

Moroz,L.A., and Yang W.H.(1980):
"Soybean trypsin inhibitor".
N. Engl.J. Med. 302:1126.

Mortimer,E.R.(1961):
"Anaphylaxis following ingestion of soybean".
J. Pediatr. 58:90.

Moxey,P.C. and Trier,J.S.(1975):
" Structural features of the mucosa of human fetal
small intestine".
Gastroenterology 68:1002.

Nasr,S.,Altman,A.B.,Meltzer,H.Y.(1981):
" Concordance of atopic and affective disorders".
J.Affect. Dis.3:291.

Neffen,H.,Oehling,A. and Subira,M.L.(1981):
" A study of the protective effects of ketotifen
in food allergy".
Allerg. Immunopathol.8:97.

Nizami,R.M.,Lewin,P.K., and Baloo,M.T.(1977):
" Oral cromolyn therapy in patients with food allergy".
Ann. Allergy 39:102.

Novey,H.S.,Fairshter,R.D.,Salness,K., Simon,R.A. and Curd,J.G.(1983):
" Postprandial exercise-induced anaphylaxis".
J.Allergy Clin. Immunol.71:498.

Ortolani,C.,Pastorella,E.,Luroghi,M.T., Torre,F.D. Bellani,M. and Zanussi,C.(1984):
" Diagnosis of intolerance to food additives".
Ann. Allergy 53:587.

Papageorgiou ,N.,Lee.T.H.,Nagakura,T., Cromwell,O., Wraith,D.G., and Kay,A.B.(1983):
"Neutrophil chemotactic activity in milk-induced asthma ".
J. Allergy Clin. Immunol.72:75.

Parish,W.E.,Barrett,A.M.,Coombs,R.R.A., Gunther,M. and Camps,F.E.(1960):
" Hypersensitivity to milk and sudden death in infancy".
Lancet 2: 1106.

Pearson,D.J., Rix,K.J.B. and Bentley,S.J.(1983):
" Food allergy:How much in the mind".
Lancet i: 1259.

Perkkio,M.,Savilahti,E., and Kuitunen,P.(1981):
" Mormphometric immunochemical study of jejunal biopsies from children with intestinal soy allergy".
Eur.J. Pediatr. 137:63.

Peters,G.A.(1965):
"Bronchial asthma due to soybean allergy".
Ann.Allergy 23:1970,

Plaut ,M.(1979):
" Histamine,H_1 and H_2 antihistamines, and immediate hypersensitivity reactions".
J. Allergy Clin. Immunol 63:371.

Pleskow,W.W.,Stevenson,D.D., Mathison,D.A, Simon,R.A., and Zeiger, R.S.(1982):
" Aspirin desensitization in aspirin-sensitive asthmatic patients".
J. Allergy Clin. Immunol 69: 11.

Podell,R. (1985):
" unwrapping urticaria; The role of food additives".
postgrad. Med. 78:92.

Prausnitz,C., and Kustner,C.(1921):
Studies uber die uberempfendlichkeit. Zbl Bakt Paras Infektion Hyg. I. Md. Hyg. Bakt Virosf Paras 86 :160, Quoted from Businco, L., Benincori,N. and Cantani, A (1984):Epidemology,incidence and clinical aspects of food allergy.
Ann. Allergy 53:615.

Pudd,P., Manuel,P.D., and Walker Smith,J.A.(1981):
" Anaphylactic shock in an infant after feeding with a wheat rusk. A transient phenomena".
Postgrad, Med 57:794.

Radermecker,M., Bekhti,A.,Poncelet,E. and Salmon,J.(1974):
" Serum IgE levels in protozoal and helminthic infections".
Int. Arch. Allergy 47:285.

Randolph, T.(1947):
" Allergy as a causative factor of fatigue, irritability, and behavior problems of children".
J. Pediatr. 31: 560.

Rao,D.C., Lalovel,J.M., Morten, N.E. and Gerrard,J.W.(1980):
" Immunoglobulin E revisited ".
Am.J. Hum Genet. 32:620

Reinhardt,M.C.(1984):
" Macromolecular absorption of food antigens in health and disease".
Ann. Allergy 53: 597.

Reinhardt,M.C., Paganelli,M.D., and Levinsky, R.J.(1983):
" Intestinal antigen handling at mucosal surfaces in health and disease: human and experimental studies ".
Ann. Allergy 51: 311.

Reisman,R.E.(1981):
" American Academy of Allergy position statements: Controversial techniques".
J. Allergy Clin. Immunol 67:333.

Rhodes,R.S. and Karnovsky,M.J.(1971):
" Loss of macromolecular barrier function associated with surgical trauma of the intestine".
Lab. Invest.25: 220.

Ribon,A., and Joshi, S.(1982):
" Is there any relationship between food additives and hyperkinesis".
Ann. Allergy 48:275.

Rinkel,H.J.,Randolf,T.G., and Zeller,M(1950):
Food allergy. Springfield, Illinois,1950.
Quoted from Grant C.B.S.(1979):Food allergies and migraine.
Lancet i: 966.

Rix,K.J.B., Pearson,D.J., Bentley,S.J. (1984):
" A psychiatric study of patients with supposed food allergy".
Br.J. Psychiatry 145: 121.

Roberton,D.M., Paganelli,R., Dinwiddie,R., and Levinsky, R.J.(1982):
" Milk antigen absorption in the preterm and term neonate ".
Arch. dis. Child 57: 369.

Roberts,S.A., and Freed,D.L.J. (1977):
" Neonatal IgA secretion enhanced by breast feeding".
Lancet 2: 1131.

Roberts,S. A.,Reinhardt,M.C., Paganelli,R., and Levinski,R.J.(1981):
" Specific antigen exclusion and non-specific facilitation of antigen entery across the gut in rats allergic to food proteins".
Clin. Exp. Immunol 45: 131.

Rothberg,R.M (1969):
" Immunoglobulin and specific antibody synthesis during the first weeks of life of premature infants".
J. Pediatr.75:494.

Rowe,A.H.(1931):
Food allergy. Philadelphia.
Quoted from Grant E.C.G.(1979): Food allergies and migraine.
Lancet i:966.

Rubin,M.I.(1940):
" Allergic intestinal bleeding in the newborn, a clinical syndrome".
Am. Med. Sci. 200: 385.

Rundles,C.C.,Brandeis, W.E ., Good,R.A., and Day,N.K.(1978):
" Milk precipitins, circulating immune complexes and IgA deficiency".
Proc. Nat. Acad. Sci.75:3387.

Rundles,C.C.,Brandeis,W.E., and Good,R.A.(1979):
" Bovine antigens and the formation of circulating immune complexes in selective IgA deficiency".
J. Clin. Invest. 64:272.

Saarinen,U.M., Backman,A.,Kajosaari ,M. and Simes,M.(1979):
" prolonged breast-feeding as prophylaxis for atopic disease".
Lancet 2: 163.

Saarinen,U.M., and Kajosaari,M.(1980):
" Does dietary elimination in infancy prevent or only pastpond a food allergy "?
Lancet 1: 166.

Sacho,M.I.,Jones,R.T., and Yunginger J.W.(1981):
" Isolation and partial characterization of a major peanut allergen".
J. Allergy Clin. Immunol 67:27.

Sampson,H.A.(1986):
" Differential diagnosis in adverse reactions to foods".
J. Allergy Clin. Immunol.78:212.

Sampson,H.A.,Buckley,R.H., and Metcalfe, D.D.(1987):
" Food Allergy ".
JAMA 258:2886.

Sampson,H.A. and Caskill,C.M. (1985):
" Food hypersensitivity and atopic dermatitis: Evaluation of 113 patients".
J. Pediatr. 107: 669.

Sampson,H.A., and Jolie,P.L.(1984):
" Increased plasma histamine concentrations after food challenge in children with atopic dermatitis".
N. Engl.J. Med.311:372.

Savilahti,E.(1981):
" Cow's milk allergy".
Allergy 36:73.

Schloss, O.M.A.(1911):
" Case of allergy to common foods.
Am.J.Dis. Child. 3:341.

Schlossman, A.(1905):
Ueber die Giftwirkung des artfremden Eiweisses in der Milch auf den organismus des Saeuglings, Arch. Kinder-heilkd 41:99. Quoted from Smith,J.A.W., Ford,R.P.K., and Phillips,A.D.(1984):The spectrum of gastrointestinal allergies to food.
Ann. Allergy 53:629.

Schwartz,H.J.(1983):
" Sensitivity to ingested metabisulfite: Variation in clinical presentation".
J.Allergy Clin. Immunol.71:487.

Seban,A.,Konijn,A.M. and Freier,S.(1977):
" Chemical and immunological properties of a protein hydrolysate formula ".
Am.J. Clin., Nutr.30:840.

Selner,J., Merril,M.A., Clamam,H.N.(1968):
" Salivary immunoglobulin and albumin: development during the newborn period".
J.Pediatr.72:685.

Shannon,W.R.(1921):
" Demonstration of food proteins in human breast milk by anaphylactic experiments on guinea pigs".
Am.J.Dis.Child 22:223

Shash,M.A.A.,Abd El-Hadi,K.,Diaa El Din, M. and Hussein, D.M.(1981):
Skin testing of normal children and children with allergic skin conditions ". Thesis submitted for partial fulfilment of Master Degree in Pediatrics. p.40,, Faculty of Medicine Ain Shams University.

Singer,A.D.,Hobel ,C.J., Heiner,D.C.(1974):
" Evidence for secretory IgE in utero.".
J. Allergy Clin. Immunol.53:94.

Singh,M.M. and Kay, R.S.(1976):
" Wheat gluten as a pathogenic factor in schizophrenia"..
Science 191:401.

Sleigh,G. and Ounsted,M.(1975):
" Present day practice in infant feeding".
Lancet. 1:753.

Smith ,W.J.A., Ford, R.P.K. and Phillips,A.D (1984):
" The spectrum of gastrointestinal allergies to food ".
Ann. Allergy 53: 629.

Soothill,J.F.(1984):
" Prevention of food allergic disease".
Ann. Allergy 53:689.

Speer,F.(1954):
" Allergic tension-fatigue syndrome".
Pediatr. Clin. North. Am .1:1029 .

Stevenson,D.D., Simon,R.A.,Lumry,W.R. and Mathison, D.A(1986):
" Adverse reactions to tartrazine".
J. Allergy Clin. Immunol 78: 183.

Stuart,C.A. Twiselton,R.,Nicholas,M.F., and Hide,D.W(1984):
" Passage of cow's milk protein in breast milk".
Clin. Allergy 14:533.

Subba Rao, P.V., Francis, M.N.L. and Metcalf,D.D (1983):
" An avidin-biotin micro ELISA for rapid measurement of total and allergen specific human IgE".
J. Immunol. Methods 57: 71.

Sullivan,T.J.,Yecies,L.D., Shatz,G.S .; Parker,C.W. and Wedner,H.J.(1982):
"Desensitization of patients allergic to penicillin using orally administered beta- lactam antibiotics".
J. Allergy Clin. Immunol 69:275.

Sutton, R ,Hill,D.J.,Baldo,B.A. and Wrigley,C.W.(1982):
" Immunoglobulin E antibodies to ingested cereal flour components: Studies with sera from subjects with asthma and eczema".
Clin. Allergy 12: 63.

Titus,R.G., and Chiller, J.M.(1981):
"Orally induced tolerance. definition of the cellular level".
Int. Arch. Allergy Appl. Immunol.65:323.

Truswell,A.S.(1985):
" Food sensitivity".
Br. Med. J. 291:953.

Vedanthan,P.K., Menon,M.M. Bell,T.D. and Bergin ,D.(1977):
" Aspirin and tartrazine oral challenge: incidence of adverse response in chronic childhood asthma ".
J. Allergy Clin. Immunol 60:8.

Vitoria,J.C., Camarero,C., Sojo,A.,Ruiz,A., and Soriano, S.J.(1982):
" Enteropathy related to fish, rice and chicken".
Arch. Dis. Child.57:44.

Von Pirquet,C.(1906):
Allergie, Munch Med. Wschr.53:1457.
Quoted from Grant,E.C.G (1979):"Food allergies and migraine.
Lancet i:966.

Walker,J.A.(1982):
Cow's milk intolerance as a cause of post-enteritis diarrhea".
J. Pediatr. Gastroenterol. Nutr.1:163.

Walker,W.A.(1977):
" Development of intestinal host defense mechanisms and the passive protective role of human milk".
Mead Johnson Symp. Perinat. Dev. Med.11:49.

Walker,W.A.(1978):
" Antigen handling by the gut ".
Arch. Dis. Child 53: 527.

Walker,W.A. and Bloch, K.J.(1983):
"Gastrointestinal transport of macromolecules in the pathogenesis of food allergy."
Ann. Allergy 51:240.

Warshaw,A.L., Walker,W.A., and Cornell,R.(1971):
" Small intestinal permeability to macromolecules: transmission of horseradish peroxidase into mesenteric lymph and portal blood".
Lab. Invest.25: 675.

Weck,A.L(1984):
"Pathophysiologic mechanisms of allergic and pseudoallergic reactions to foods, food additives and drugs".
Ann. Allergy 53: 583.

Weil,G.J., Hussain,R., Kumaraswami,V. , Philips,K.S. and Ottesen,E.A(1983):
" Prenatal allergic sensitization to helminth antigens in offspring of parasite-infected mothers".
J. Clin. Invest.71:1124.

Wilson,S.J. and Walzer,M.(1935) :
" Absorption of undigested proteins in human beings: Absorption of unaltered egg protein in infants and children".
Am.J. Dis. Child 50:49.

Wood,C.B.S(1984):
Food allergy, Chapter 4. In" Recent advances in Pediatrics", edited by Meadow, R.p.57.
Churchill Livingstone. Edinburgh.

Wood,C.B.S.(1986):
" How common is food allergy"?
Acta Pediatr. Scand.323:76.

Wurtman,R.J.(1983):
" Food consumption, neurotransmitter synthesis and human behavior".
Experientia. 44:356.

Yunginger,J.W.(1986):
"Proper application of available laboratory tests for adverse reactions to foods and food additives"
J. Allergy Clin. Immunol 78:220.

Zeiger,R.S.,Heller,S., Mellon ,M., Conner R., and Hamburger R.N.(1986):

" Effectiveness of dietary manipulation in the prevention of food allergy in infants".
J. Allergy Clin. Immunol.78:224.

ARABIC SUMMARY

الاضطرابات الناتجة عن حساسية الطعام فى الاطفال ، بالاشارة الى التغيرات السلوكية

تعتبر امراض الحساسية والتى غالبا ما تظهر اثناء الطفولة من الاسباب الهامه للتردد على عيادة اطباء الاطفال ومن الممكن ان تصبح مشكلة طوال العمر .

وتعتبر الحساسية من الاسباب الرئيسية للامراض الحادة والمزمنة فى الاطفال ، ولقد اثبتت الدراسات ان ٢٠٪ من الاطفال (من سن الولادة وحتى ١٧ عاما) يعانون من امراض الحساسية .

والحساسية الناتجة عن الطعام تمثل بعض المشاكل الرئيسية لكثير من الناس .. وعلى الرغم من ان نسبة حدوث حساسية الطعام غير معروفه على وجه الدقة الا انه يمكن تقديرها فى الاطفال بحوالى ٣ر٪ الى ٥ر٧٪ ، وتقل هذه النسبه تدريجيا مع السن .

وفى قديم الزمان ، حكيم الطب ابيو قراط (٤٦٠ ـ ٥٧٠ قبل الميلاد) وجالن (١٣٠ ـ ٢١٩ بعد الميلاد) اول من وصفوا الجوانب الاكلينيكية لالبان الابقار والماعز .

اما اول من ذكر الحساسية للطعام فهو الشاعر اللاتينى "لوكريتيوس" فى القرن الاول من الميلاد . وفى القرن الحالى فان اهمية الحساسية للطعام فى سن الطفولة قد نالت اهتماما بحثيا وخاصة فى السنوات العشر الاولى من القرن العشرين .

وقد خلصت عدة دراسات خلال الثمانينات الى ان الحساسية الناتجة عن الطعام تلعب دورا جوهريا فى حالات الارتيكاريا والاكزيما والاضطرابات الداخلية لبروتين لبن البقر والتهابات القولون عند الاطفال وكذلك المغص والصداع النصفى وزيادة الحركة فى حين ان الازمات الربوية وامراض التهابات الامعاء احيانا تكون ذات صلة وثيقة مع تفاعلات الحساسية الناتجة عن الطعام .

والاضطرابات المعدى معوية الناتجة عن حساسية الطعام تظهر اكثر وضوحا فى الاطفال حيث ان مكونات اللبن ممكن ان تسبب هذه الاضطرابات . ودخول الطعام

المسبب الى المعدة ثم الى الامعاء من الممكن ان يسبب غثيان وتقلصات والم وانتفاخ فى الامعاء والقىء والاسهال .

والحساسية الناتجة عن الطعام ممكن ان تظهر فى اكثر من نسيج من أنسجة الجسم خارج الامعاء . ويعتبر الجلد من الانسجة الاكثر شيوعا لظهور الاعراض فى صوره الارتيكاريا الحادة والمزمنة والاوديما الوعائية العصبية . كما انه انتشار مرض الاكزيما كنتيجة للحساسية للطعام تم اثباته تجريبيا .

والازمات الصدرية (الربوية) والتهاب الاغشية المخاطية للانف والتى تحدث نتيجة للحساسية للطعام اكثر شيوعا فى الاطفال عنها فى الكبار . والاعراض الانافيلاكتية الناتجة عن الحساسية للطعام ممكن ان تحدث خلال دقائق من تناول الطعام او فى بعض الحالات خلال ساعات .

واظهر جرانت سنة ١٩٧٩ بان حساسية الطعام تلعب دورا رئيسيا فى نشأة الصداع النصفى كما ان مونرو وآخرين اثبتوا ان التفاعلات الناتجة عن حساسية الطعام هى المسبب للصداع النصفى .

وبين كتير وبالدوين ان الحساسية الناتجة عن الطعام من الممكن ان تزيد من خطورة الخلل الوظيفى السلوكى للاطفال المصابين بالحد الادنى للخلل الوظيفى للمخ .

وقرر ميلمان وآخرين ان الجمع بين العلاج النفسى وعلاج الحساسية قد حسن الاداء المدرسى والسلوك لسلسلة من الاطفال غير القادرين على التعلم .

ويمكن تعريف الحساسية الناتجة عن الطعام بانها التفاعلات المناعية الناتجة عن هضم الطعام او مضيفاته .

كما أن العوامل الوراثية تلعب دورا هاما فى حدوث الحساسية ، وتأكيدا لذلك فان الدراسات الاحصائية للاطفال من سن ٢ : ٤ سنوات والمنتسبين لاباء يعانون من الحساسية، أظهرت أن احتمال الحساسية يصل من ٥٠٪ الى ٥٨٪ بافتراض

ان احد الابوين يعانى من الحساسية وتصل من ٦٧٪ الى ١٠٠٪ فى حالة ما اذا كان كلا الابوين يعانى من الحساسية .

والدراسات التى اجريت على الاطفال اوضحت ان نقص الجسم المناعى من فصيلة " أ" والاطفال المبتسرين والاصابه بالطفيليات ونوع الغذاء فى الشهر الاول بعد الولادة ، كل هذه العوامل تؤثر تأثيرا واضحا على التقاط خلايا الامعاء للجسم المسبب للحساسية .

وقد اثبتت التجارب ان لبن الام يقلل من حدوث الحساسية عن طريق تجنب التعرض الى وتقليل امتصاص الامعاء للعامل المسبب للحساسية . كما انه تم التدليل علميا على ان الاجسام المناعية فى لبن الام وخاصه الفصيلة " أ" لها أثر فعال فى منع امتصاص العامل المسبب للحساسية فى الطعام وحماية الامعاء .

كما ان الامهات اللاتى يرضعن اطفالهن عن طريق الرضاعة الطبيعية عادة ما يؤخرن اعطاء اولادهن الغذاء الجاف ويعنون باطفالهن عناية اكبر . كما انهن يدخن اقل .

وقد خلصت الدراسات الى ان لبن الام يقلل من حدوث حساسية الطعام عن طريق عاملين هامين وهما طول فترة الرضاعة الطبيعية لسته اشهر على الاقل وتأخير اعطاء الاغذية الجافة .

وفى سن الرضاعة والطفولة المبكرة فقد وجد ان لبن البقر وبروتين الصويا وكذلك البيض والقمح والارز والسمك ولحم الدجاج والشعير بالاضافه الى الطماطم والبرتقال والموز والشيكولاته قد سببوا اعراض معدى معويه فى بعض الاطفال .

والطعام بصفه عامه يؤثر على السلوك عن طريق تغيير مستوى الناقلات العصبية فى الجهاز العصبى المركزى وقد اوضحت الدراسات ان حساسية الطعام تسبب الضعف التوترى الناتج من الحساسية ، والذى يتكون من التوتر ، الضعف ، عدم الاحساس بالراحة ، الاحلام المزعجة ، والصداع .. كما انها تسبب النشاط الحركى الزائد

وفقد الانتباه . وعادة ما تصاحب هذه الاعراض بالسلوك العدوانى والقابلية للاثارة والتى تؤدى الى مشاكل اجتماعية وتعليمية خطيرة وتصل نسبتها الى ٥ ٪ من الاطفال فى سن ما قبل المدرسة .

ولتشخيص الحساسية للطعام يجب اجراء تقصى وتأريخ دقيق للاعراض الاكلينكية لكل حالة على حدة ويجب اجراء فحص جسمانى دقيق وكذلك اختبارات معملية ، واختبارات مناعية ، كالاختبار الجلدى واختبارات الكشف عن الاجسام المناعية والكشف عن الهستامين واختبار تجنب الاطعمة المسببه ثم اختبار الغذاء المنظم .

والعلاج الامثل للحساسية للطعام هو تجنب العامل المسبب ثم يأتى العلاج عن طريق استخدام العقاقير ثم العلاج عن طريق تخفيض مستوى الحساسية للعامل المسبب .

وللوقاية من حدوث الحساسية للطعام يجب اتخاذ اجراءات مبكرة حتى نحصل على افضل النتائج والتوصيات الخاصه والتى تساعد على تقليل حدوث الحساسية للطعام للاطفال المعرضين يمكن اجمالها فيما يلى :

١ - تجنب الاطعمة المعروفة بتسببها فى احداث الحساسية للطعام خلال الفترة من السنة الاولى الى الثلاث سنوات الاولى من العمر . وكذلك تجنب المستنشقات المسببه للحساسية بصفه عامه .

٢ - التوصيه بالرضاعة ، بلبن الام لاطول فترة ممكنة وعلى الاقل لمدة سته أشهر .

٣ - الوجبات المكملة من طعام فول الصويا ولبن البقر يجب تجنبها خلال السنة الاولى .

٤ - استعمال البان بديلة تمتاز بقلة احداثها للحساسية مثل لبن " نيوترامجن "

٥ - تجنب الام الاطعمة المسببه للحساسية اثناء فترة الرضاعة وخلال الثلاثة أشهر الاخيرة من الحمل .

٦ - عدم اعطاء الطفل الاغذية الجافة والاطعمة المسببه للحساسية اثناء اصابة الطفل بالاسهال .

٧ - الاطعمة المعروفة بقلة تسببها فى الحساسية تضاف تدريجيا من سن ٦ أشهر الى ١٢ شهرا ولبن البقر يضاف بعد سن سنه من العمر ثم اضافة القمح والذرة والشعير تدريجيا ثم البيض عند سن سنتين ثم البقول والاسماك عند سن ٣ سنوات .

٨ - تزويد الام بقدر كاف من الكالسيوم والفيتامينات .

٩ - تقييم الطفل عند سن ٤ اشهر ثم سنه ثم سنويا بعد ذلك حيث ان اكتشاف الحساسية مبكرا يمكن ان تعطى نتائج افضل فى العلاج .

١٠ - تجنب اعطاء مصل ضد الدفتريا والتيتانوس والسعال الديكى خلال اسبوعين من اجراء الاختبار الجلدى .

١١ - استعمال بعض العقاقير فى حالة عدم القدرة على تجنب الطعام المسبب للحساسية .

الاضطرابات الناتجة عن حساسية الطعام فى الاطفال بالاشارة الى التغيرات السلوكية

72
5
٦٢

رسالة مقدمة من

الطبيب / أبو المجد أحمد عبد الرحيم فرغلى

تمهيدا لنيل درجة الماجستير فى دراسات الطفولة

قسم الدراسات الطبية

تحت اشراف

الاستاذ الدكتور

ضيائى حسين

أستاذ طب الاطفال

الدكتور

عمر السيد الشوربجى

مدرس بمعهد الدراسات العليا للطفولة

قسم الدراسات الطبية

معهد الدراسات العليا للطفولة

جامعة عين شمس

١٩٨٨