REVIEW OF LITERATURE
REVIEWS OF LITERATURE

Von Pirquet (1906) coined the term allergy for a 'state of changed reactivity in a host, occurring as a result of contact with a foreign substance. He put together the Greek words "allos" meaning different or changed and 'ergos' meaning work or action. This altered reactivity could either be beneficial to host as in the case of immunity or detrimental as in anaphylaxis. In modern usage allergy refers only to adverse effects.

ONTOLOGY OF IMMUNE SYSTEM

The immune system arises from developing lymphoid tissue during embryogenesis. The lymphoid tissues are of two types i.e. central and peripheral. In our case the central lymphoid organ is the thymus.

In humans B cell (Bursa dependent) are involved in humoral or antibody mediated immunity and T cells (Thymus dependent) involved in cell mediated immunity. Their differentiation occurs in thymus and probably gets stimulated by a humoral factor produced by the thymic epithelium termed as thymopoietin or thymosin (Goldstein et al, 1974)

Hall (1974) proposed that T cells migrate from the thymus by way of blood stream and lymphatics to populate the peripheral lymphoid organs i.e. lymphnodes, spleen, bone marrow, tonsils and gut associated lymphoid system.
Gathings and Cooper (1977) observed that B cells precursors are demonstrable in the mammalian fetal liver and adult bone marrow.

Pearl (1978) opined that migration of B cell to the peripheral lymphoid organs also occurs.

Pierce and Kapp (1978) postulated that a third lymphoid cell evolving from the central stem cell line during this period is the monocyte or in it's mature form macrophage and over the past several years it has been recognised that interaction of macrophage with T and B cells is important in the initiation of immune response and it's regulation.

HUMORAL IMMUNITY

Stimulation of the production of specific antibodies depends upon the nature of antigen. Antibody activity in humans reside in five major classes of globulins. These immunoglobulin classes are termed as IgG, IgM, IgA, IgD and IgE. Each immunoglobulin class appears to be synthesized by a separate B cells subclass. It has been recognised that for maximal B cell IgM and IgG primary responses to occur to most antigens, the presence of T cells is required (Katz et al, 1972). This population of T cell is known as Helper T cells (Friedman and Greaves, 1973).

In contrast to the majority which are T dependent antigens, there are a few antigens which do not
require mediation by T cells. These are called as T independent antigens (Moller, 1973).

Along with the interaction of B and T lymphocytes, macrophages also play a vital role. Initially antigenic proteins bind to macrophage before their recognition by T lymphocytes (Basten et al, 1976).

Benacerraf (1978) suggested that macrophage process or degrade the antigen and then the antigen is combined with a product of genes which are linked to the histocompatibility complex (MHC) of the species. This gene product was called Ia or Immune Response Associated, presumably coded for by a corresponding Ir or Immune Response Gene.

Again Benacerraf and Germain (1978) wrote that the combination of processed antigens and Ia was presented to T cell for immune recognition and stimulation to helper activity or effector activity.

Seligmann and Franklin (1978) suggested that B lymphocytes have readily identifiable IgD and IgM monomer present on their cell membrane.

REGULATION OF ANTIBODY SYNTHESIS

It is known that following the interaction of macrophages, helper T cells and B cells, the B lymphocytes undergo blastogenesis and are transformed into mature plasma cells, which synthesize specific class immunoglobulin. Many regulatory mechanisms, however, operate over this.
IgM B cells are suppressed by circulating IgG antibody directed against the same antigenic specificity (Sercuz et al, 1974).

There is a growing evidence that suppressor T cells exert a regulatory effect and yet another T cell subpopulation may exist, generating an opposing amplifier signal to which, the mature B cells is subjected (Markham et al, 1977).

Thus, amplifier and suppressor T cells appear to generate complementary effects to keep the degree of B cell activity appropriate to antigenic stimulation (Benacerrag, 1978).

Macrophages also exert modulatory influence on B cell biosynthesis mediated by elaboration of so called monokine which enhances antibody formation (Dimitriu and Faucl, 1978).

Populations of suppressor T cells regulate IgA and IgE synthesis also. Initiation of a specific IgE response is dependent on interaction between the macrophage, helper T cells, and IgE B cell analogous to the IgG response.

**IMMUNOGLOBULINS**

Immunoglobulins are a heterogeneous group of proteins belonging to gammaglobulin fraction of the serum proteins. Their main function is to act as antibodies.
The gammaglobulins were first designated by Tiselius in 1937 as a distinct group of serum proteins having a distinct electrophoretic mobility.

Kunkel and Putnam (1953) showed that myeloma proteins in the serum of patients with multiple myeloma belonged to gammaglobulin fraction of serum proteins.

Graber et al (1953) supported the finding of Heidelberger and also separated the newer IgA besides the IgM and IgG by an immunoelectrophoresis technique.

Porter (1959) was able to clear the immunoglobulins into two fragments, separable by ion exchange chromatography; one fragment retained the capability to react with the immunogen and was called Antigen binding fragment or Fab, the other crystallized upon standing and was called crystallizable fragment or Fc.

According to Edelman and Poulak (1961), globulin could be split into two components by reduction with thiols in the presence of urea i.e. the heavy chains (Molecular weight 50000) and light chain (molecular weight 20,000).

Grey and Kunkel (1964) discovered the subclasses of IgG, viz. IgG₁, IgG₂, IgG₃ and IgG₄.

Rowe and Fahey (1965) discovered the fourth class of immunoglobulins viz. IgD from an atypical myeloma protein.

Kunkel and Prendergast (1966) discovered the subclass of IgA.
IgE

In 1967, Ischizaka et al discovered that reagents or skin sensitizing antibody belonged to a unique class of immunoglobulin which they called IgE and it remained as a principals if not the sole mediator, of type I hypersensitivity reaction.

Johansson et al (1970) found that IgE level varied with age but not with sex. Patients with asthma and atopic dermatitis had raised IgE level more often than patients with allergic rhinitis. Atopic dermatitis had the highest mean IgE level.

Tada (1975) found that 1% of the total IgE was cell bound.

In 1975, Norman suggested that IgE was the principal mediator of immediate (type-I) hypersensitivity reactions.

IgE binds to tissue mast cells and basophils. This cell bound complex then causes degranulation of basophils on combining with antigen (allergen), with the result histamine and other mediators are released (Beaven, 1976).

Homburger (1978) suggested that IgE concentration was generally higher in the allergic population, although there was some overlapping with non atopics.

Biological properties of IgE class were investigated and presented by Ishizaka et al (1978).
Zeiss (1980) discovered that Fc fragment of immunoglobulin was responsible for the protein's ability to fix to receptors on mast cells and basophils.

Leung et al in his review (1985) concluded that T lymphocytes played an important role in the isotype specific regulations of the human IgE response.

**CELL MEDIATED IMMUNITY**

Parker (1976) concluded that the parallel mechanism of immune recognition and immune regulations were analogous in humoral and cell mediated immunity. However, immune reaction in cell mediated immunity was brought about by sensitized lymphocytes, rather than by free antibody molecule.

The development of antigen specific T lymphocyte is dependent on interaction of macrophage and T cell.

Benner and Van Ouden aren et al (1977) showed that memory T cells were long lived and maintained immunologic memory of previously encountered antigens.

Kapp et al (1978) postulated that suppressor T cells were responsible for establishing tolerance to self antigens.

Effector T cells, on contacting with antigen created the molecular, cellular and clinical manifestation of cell mediated immunity reaction (Binz, 1978).
CLASSIFICATION OF HYPERSENSITIVITY REACTIONS

Gell and Coomb (1963) classified the immune response into four types i.e. type I to IV hypersensitivity reactions, of which type I is known as anaphylactic or reagin dependent. Several modifications however have been proposed to the Gell and Coomb classification system (Sel1, 1975).

Raitt (1972) added fifth category of immune response i.e. stimulating antibody reaction and Irvine (1984) described the sixth i.e. antibody dependent cell mediated cytotoxicity (ADCC).

TYPE - I : ANAPHYLACTIC REACTION

This type of reaction is also called immediate type hypersensitivity or reaginic hypersensitivity and is caused by reaginic antibody of the IgE class (IgE₄ in a few cases) e.g., extrinsic bronchial asthma, allergic rhinitis, partly atopic dermatitis, most cases of anaphylactic shock, some cases of urticaria and angio-edema (Lakin and Cahill, 1976).

Antigens which cause type-I reaction are called allergens. When the allergen reacts with IgE attached to the surface of the mast cells, the cell degranulates and liberates chemical mediators, responsible for symptoms.

Main chemical mediator is histamine and others are SRS-A (Leukotriene C₄+D₄+E₄), leukotriene B₄, ECF-A (eosinophil chemotactic factor of anaphylaxis), platelet
activating factor (PAF), TxA₂, a high molecular neutrophil chemotactic factor (MCF) and prostaglandin D₂ (Mathe et al., 1977).

In 1978, Lichtenstein concluded that these chemical mediators were responsible for vasodilation, increased capillary permeability, and smooth muscles contraction, which were manifested clinically as urticaria angioedema, hypotension, bronchospasm, spasm of gastrointestinal musculature, or uterine contractions, depending on the location and severity of the reaction.

In contrast to other cell types, mast cell and basophils have high affinity receptors for IgE, these are about 10⁵ per cell.

**TYPE-II : CYTOTOXIC REACTION**

This reaction is also termed as complement dependent cytotoxicity. Complement system also mediates type III or toxic complex reaction.

**TYPE-III : TOXIC COMPLEX REACTION OR IMMUNE COMPLEX REACTION**

In this reaction, complexes are formed between circulating antigen and specific antibody, especially of IgE class. In this reaction complement system is also activated, causing local infiltration by neutrophils, which in turn release tissue damaging enzymes.

Dixon (1965) concluded that arthus reaction experimental and clinical serum sickness, few glomerulo-
nephritis and some drug reactions, followed the mechanism of type III reaction.

Fink and Salvaggio (1978) thought that type III reaction played a significant role in the pathogenesis of various hypersensitivity pneumonias.

**TYPE - IV : CELLULAR HYPERSENSITIVITY REACTION**

This is also called delayed hypersensitivity reaction, as a delay of 24 to 72 hours occurs in the initiation of reaction and is mediated by antigen specific sensitized T lymphocytes. Sensitized T lymphocytes also act by liberating lymphokines, which mobilize non sensitized cells to fight the antigen.

David et al (1964) observed as little as 2.5% antigen specific T lymphocytes to the total cell population, in the delayed reaction.

**TYPE - V : STIMULATING ANTIBODY REACTION**

This reaction was considered as a modification of the type II reaction, by Raitt (1972), in that the specific antibody combines with antigen on the cell surface but complement was not activated.

The classical example of this reaction is in Graves' disease (Exophthalmic Goitre) in which excess amounts of thyroid hormones are produced.

**TYPE - VI : ANTIBODY DEPENDENT CELL MEDIATED CYTOTOXICITY (ADCC)**

K cell mediated cytotoxic mechanisms may be important in the pathogenesis of auto-immune disease and
in tumour rejection. K cells were also involved in the defence against helminthic infections such as schistosomiasis where the size of the parasite is too large for effective phagocytosis.

**DIAGNOSIS OF ALLERGY AND HYPER-REACTIVITY**

It was earlier believed that allergy was the cause of almost all cases of asthma, rhinitis and dermatitis. When an allergen could not be identified, bacterium, food, or yet unidentified substance was incriminated. However, it has been realized that increased non-specific responsiveness of the diseased organ, hyper-reactivity, is of considerable importance (Cockroft, 1983).

For the diagnosis of allergy and hyper-reactivity, following points are considered (Mygind Niels, 1986):

1. History
2. Physical examination
3. Exercise test
4. Histamine test
5. Blood eosinophil count
6. Total serum IgE
7. Skin testing with appropriate allergen
8. RAST

In 1921 Prausnitz and Kustner for the first time demonstrated transfer of immediate hypersensitivity from an affected individual to a normal individual through serum.

Atopy and atopic refer to certain allergic diseases which have a familial tendency to occur and are associated with eosinophilia of blood and tissue secretions (Coca, 1923).
In 1925, Coca and Grove did extensive studies of skin sensitizing factors from the sera of the patients with ragweed hay fever.

The cutaneous reactivity of infants and neonates is reduced (Sulzberger et al., 1940; Matheson et al., 1954 and Kaufman, 1971).

Herzheimer et al (1954) studied and evaluated the role of skin test in respiratory allergy.

Chambers et al (1958) showed that asymptomatic subjects, who are skin test positive (ragweed pollenosis) are at a higher risk of developing an allergic syndrome, if less than the 40 years of age, as compared to subjects who are skin test negative.

Curran and Goldman (1961) found 50% of the non-allergic individuals with a positive family history of atopy and positive skin tests to aeroallergens, compared to only 9% of subjects with a negative family history.

In 1965 Reinberg et al demonstrated that skin reactivity to histamine and to compound 48/80 was maximal between 7 to 11 PM and was at its nadir at 7 AM.

Morrow Brown et al (1968) studied the role of mites in house dust, by skin testing. They found that dermatoptagoides, pteronyssinus played an important role in sensitizing susceptible people. Hence the use of mite extract was considered to be an important advance in the diagnosis of allergy to house dust. They also found in their study that in 50% cases, there was no history to
suggest house dust sensitivity, especially in children, but nasal provocation tests were all positive.

Morrison Smith et al (1969) in their study, 'clinical significance of skin reactions to mite extract in children with asthma found that more than 50% of school children in Birmingham suffering from asthma showed positive prick test reactions to house dust, but these reactions were small and relatively less frequent than prick test reactions to gross pollen in children with pollen allergy. Though positive reactions to D. pteronyssinus were obtained more frequently and were of greater size than those from other extracts, it was considered that D. farinae was a suitable substitute for D. pteronyssinus for skin testing.

Hagy and Sethipane (1969) in their study showed that skin test reactivity in the range of 20 to 49% was present in the general population.

Louse and Lubs (1971) concluded that allergic diseases had both environmental and hereditary factors operating but environmental factors were predominant. This was shown by low concordance in the monozygotic twin group (25.3%) and in the dizygotic group (16.1%).

Study of Lal et al (1973) showed that there was a high incidence of positive skin reactions to extracts of both mites and house dust in individuals with extrinsic bronchial asthma. These reactions showed a significant correlation with the clinical history of house dust
allergy and bronchial asthma. The presence of mites in 19 out of the 25 samples analysed and positive skin test clearly suggested that the house dust mite of dermato-phagoides species was present in this part of the world and was playing a significant role in the etiopathogenesis of bronchial asthma.

Gleich et al (1974) noted the highest allergen specific IgE levels between 12 and 20 years of age.

Hendrick et al (1975) had reported decreased prevalence of skin reactivity with age. Peak skin test reactivity has previously been reported to be the highest in 15 to 30 years old age group (Pearson, 1987).

Barbee et al (1976) believed that sensitivity of skin tests was decreased in the elderly,

Godfrey et al (1976) evaluated the prevalence of immediate positive skin test to D. pteronyssinus and grass pollen in school children. The range of prevalence for positive skin tests in allergic population was 50 to 95%.

Lee et al (1977) confirmed the observations to skin test responses to grass and house dust extracts. They suggested that false negative readings could result if skin tests were performed in the early morning office hours.

Cavanaugh et al (1977) evaluated the clinical values of bronchial provocation testing in childhood asthma.
Skin test reactivity was positively correlated with total IgE and specific serum IgE levels (Pascual and Reddy et al, 1977).

In 1978, Reddy et al, made a re-appraisal of intercutaneous tests in the diagnosis of reaginic allergy. Skin test reactivity to an allergen was also highly correlated to both basophil sensitivity and tissue (bronchial nasal)sensitivity to that allergen (Cockcroft et al, 1979).

Brown et al (1979) studied the relationship of skin test reactivity and serum IgE in cases of respiratory allergy.

Skin tests were used to diagnose allergic disorders in infancy (Businco et al, 1979; and Warner, 1980).

Prick tests are totally harmless in infancy and the reproducibility may be improved by the use of the recently standardized devices (Nelson, 1983).

The skin prick test is more sensitive than the scratch test. Intradermal skin testing is higher in sensitivity but less specific than epicutaneous skin test. Thus, a greater number of false positive reactions can occur in intradermal skin testing. In circumstances where intradermal tests may be dangerous (certain foods and drug allergens), skin prick testing is particularly useful as the initial form of allergy testing (Krouse et al, 1980; Brown et al, 1981; Robert et al, 1983).
Ellis (1983) defined the role of complement in atopic diseases.

According to Position, Statement of the Practice Standards Committee (1983), the skin tests appear to be superior to currently available RASTS in the diagnosis of certain life threatening anaphylactic states in which maximum sensitivity is important, particularly in the diagnosis of penicillin and Hymenoptera allergy. The results of skin tests are more immediately available. Where both tests can be initiated at the time of the patient's visit the result of skin tests are available in about 45 minutes, those of RASTS are available in 2 to 3 days. RAST is preferable to skin testing in certain conditions where skin testing is unsatisfactory, particularly where there is dermatographia or widespread skin disease.

Allen D. Adinoff et al (1983) observed that skin testing was standard clinical method for demonstrating the presence of allergen specific IgE antibody in allergic diseases.

According to Anderson (1984) non-immunologic mechanisms also played a role in the pathogenesis of atopic disease.

There was a good correlation between IgE, FAST test, RAST and skin testing (Tsay et al, 1984; and Mirone et al, 1987).
According to Menardo et al (1985) skin test reactivity to histamine and mast cell degranulating agents was lower in newborn infants as compared to adult.

Skin tests represented a major tool in the diagnosis of immediate type allergy (Skassa-Brociek et al, 1985).

Diminished end organ responsiveness in infants and elderly individuals to inflammatory mediators appear to be one contributory mechanism for decreased prevalence of allergen skin test reactivity at extremes of age (Van Asperen et al, 1985).

Jean Luc Menardo et al (1985) studied and confirmed that prick tests could be performed and interpreted without difficulty in infants, keeping in mind that small wheal size was produced by both positive control solutions and allergens.

Rosario Scolozzi et al (1987) believed that presently no in-vitro technique was as sensitive as skin test for allergen specific diagnosis of inhalant allergic disease,

Nalebuff et al (1989) suggested that skin test was more sensitive, faster and relatively less expensive in comparison to RAST.

Pakit Vichyamond et al (1989) observed in their study, that there was no difference in wheal and erythema sizes between morning versus evening skin testing.
Hattevig et al (1989) noted a decreased incidence and severity of atopic dermatitis in first 6 months of life, if the lactating mothers avoided eggs, cow's milk and fish during the first 3 months of breast feeding.

**Spectrum of Illness: Bronchial Asthma**

Asthma represents most serious but common allergic condition of childhood. The term asthma is derived from Greek word meaning "Struggling for breath". There is no universally accepted definition of asthma.

Bruce (1958) observed that nearly 50% patients of asthma had family history of allergy.

In 1964, Vishwanath defined that bronchial asthma is a syndrome that is characterised by attack of expiratory dyspnoea, not attributable to disease of the heart or the lung. The smooth muscles in the bronchi and bronchioles exhibits spasm, edema and exudation following exercise, natural exposure to strong odour, irritant, fumes, tobacco, smoke, cold air, intensional exposure to parasympathomimetic agents.

Bronchial asthma may be regarded as diffuse obstructive lung disease with hyper-reactivity of the airways to variety of stimuli and high degree of reversibility of obstructive process which may occur either spontaneously or as a result of treatment.

In 1964, Rockeman divided asthma into extrinsic asthma and intrinsic asthma. Differences were described as follows:
<table>
<thead>
<tr>
<th></th>
<th><strong>Extrinsic</strong></th>
<th><strong>Intrinsic</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of onset</td>
<td>3-35 years</td>
<td>≤3 and 735 years</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Seasonal and perennial</td>
<td>Increased in winter, increased by cold air, infection, pollution.</td>
</tr>
<tr>
<td>Mucus</td>
<td>Clear &amp; foamy</td>
<td>Thick and white or colourless</td>
</tr>
<tr>
<td>Atopy</td>
<td>Positive</td>
<td>Absent</td>
</tr>
<tr>
<td>Skin test</td>
<td>Positive</td>
<td>Negative or positive—non-correlation</td>
</tr>
<tr>
<td>Serum IgE</td>
<td>High</td>
<td>Normal</td>
</tr>
<tr>
<td>Response to therapy</td>
<td>Good response to bronchodilator and immunotherapy</td>
<td>Poor response to bronchodilator, no response to immunotherapy.</td>
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Eosinophilia was reported in majority of cases of bronchial asthma by Lowell et al (1967) and Sharma et al, (1974).

Samter and Beers (1968) described a special category of non-antigenic asthma, which was induced by the ingestion of aspirin. Skin test to aspirin was always negative in these patients.

Szentivanyi's theory (1968) considered asthma to be due to abnormal beta adrenergic receptor, adenylate cyclase function with decreased adrenergic responsiveness.

William and Macnicol (1969) in his study found that 3.7% population had regular episodes of asthma from early childhood to 10 years of age. In adult the incidence of asthma was 1% of population, approximately.
Berg et al (1969) observed high serum IgE level in 90% cases of perennial asthma and 50% cases of seasonal asthma.

Gleich et al (1970) also observed high serum IgE level in allergic asthma.

Jarrett (1972) suggested that potentiation, as a result of parasitic infestation, could increase the severity of an individual's allergy by elevating specific IgE level to undesired allergens, such as ragweed pollen etc.

In 1973, Robinson suggested that the asthmatic paroxysm is triggered by the hypersensitivity reaction or by mental stress. Allergy was always a basic factor of an asthmatic paroxysm.

William and Micol (1973) observed that 90-95% of asthmatic children had atopic constitution to develop type I hypersensitivity demonstrated by skin prick testing by various allergens.

In 1973, Jarrett showed in his study that some allergic children gave positive skin test for thread worm antigen and so the author suggested that hypersensitivity to E. vermicularis allergen absorbed from the bowel might contribute to the allergic signs and symptoms. There was no effect of treatment.

Parker and Smith (1973) thought that the decreased beta adrenergic receptor on leukocyte, of non adrenergic
drug treated asthmatics may provide the morphological basis for the observed hyporesponsiveness to beta agonist.

Alternatively increased cholinergic activity in the airways had been proposed as fundamental defect in asthma, perhaps due to some intrinsic or acquired abnormality in irritant receptors which seem in asthmatics to have lower threshold for response to stimulation (Nadel, 1977).

Gupta et al (1975) observed eosinophilia irrespective of the type of asthma in their study.

Lee and associates (1976) observed that about 11% of population have asthma by 3 years of age.

Agrawal et al (1979) reported significantly high absolute eosinophil count (917.71±618.9) in cases of bronchial asthma compared to control (231.4±105.4).

A role of viral infections in the allergic sensitization process has been postulated by Frick, German and Mills (1979) who studied 13 children with 2 allergic parents, 11 developed clinical allergy and five developed asthma after an attack of respiratory viral infection.

Eosinophil in intestinal parasitic infestation not only involved quantitative change in eosinophil numbers but also a qualitative change in functional capacity that rendered circulating eosinophils more efficient in resisting parasitic infestation. David et al (1980) proved this by showing increased capacity of eosinophils to kill schistosoma mansoni larva in vitro.
Sims et al (1981) observed that about 5% of children suffered from frequent wheezy episodes at some time in their childhood and incidence increased to 20% if children having less than 6 attacks of wheezing were included. It was also observed that about half of the children presenting with asthma were atopic and associated with common minor immunodeficiencies. This disease started at any age; about 80 to 90% of asthmatic children had their first attack before the age of 5 years.

Lukza et al (1982) found eosinopenia in case of acute asthma and eosinophilia in cases of chronic and stable asthma.

Eosinophilia in varying degree, 30 to 40% was also reported by Archarya (1963) in their study of childhood asthma.

Prior to puberty about twice as many boys as girls were affected, thereafter the incidence of sex was equal (Ellis, 1983).

Paihi et al (1990) showed agreement between a history of asthma with allergy to house dust and bronchial challenge to whole house dust. All allergic patients had significant bronchoconstriction whereas no reaction could be elicited in the non-allergic group.

ALLERGIC RHINITIS

Seasonal allergic rhinitis is a symptom complex seen in children who have become sensitised to wind borne
pollen of trees, grasses and weeds. It is characterized by watery rhinorrhea, nasal congestion, sneezing and itching of eyes, nose and throat.

Connell (1969) defined that there may occur inflammation following the acute phase reaction due to hyper reactivity of allergic nose to a variety of non-specific stimuli such as cigarette smoke, strong odours, air pollution and climatic changes.

Phillips has shown that an individual requires two more seasons of exposure before exhibiting clinical manifestation of disease.

Cell bound IgE antibodies in response to antigenic stimulation, cause release of mediators, immune reaction and bring about manifestations of the disease (Kaliner et al., 1973).

Incidence of allergic rhinitis was reported to be 10% in general population by Viner and Jackman (1976).

Peripheral blood eosinophils of 4-8% may or may not be present in active allergic rhinitis, but characteristic eosinophils of the nasal secretions obtained during the period of symptoms may be of diagnostic value (Tennenbaum et al., 1980).

From 3-10%, patients of allergic rhinitis could develop asthma or other atopic diseases (Ellis, 1983).

According to Michael Kaliner (1987) skin testing with potent antigenic preparations and positive and
negative control substances remains the most revealing procedure in diagnosing specific allergic factors associated with allergic rhinitis.

**URTICARIA**

It consist of raised erythematous skin lesions, which are marked by pruritus.

Angioedema is characterised by asymmetrical swelling of tissue. This is like urticaria but involves deeper tissue. Urticaria and angioedema may occur together.

Triple response observed by Lewis (1927) consist of erythema due to capillary and vascular dilatation, edema due to increased capillary permeability and flare due to axon reflex. Intercutaneous injection of histamine inflicts similar type of response along with pruritus implicating that histamine mediates the urticarial response.

Temperature changes induce urticaria with considerable frequency. Idiopathic acquired cold urticaria is probably the most common example of this (Anderson, 1967). Pasricha (1972) undertook the study to ascertain how far gastrointestinal parasites were responsible for producing urticaria.

Mathews (1974) concluded that nearly 20% population at some time in life suffer from some form of urticaria.

Acute urticaria persists less than 6 weeks while episodes which lasts more than 6-8 weeks are referred as
chronic urticaria. Pathogenesis is mediated by histamine release.

Habte Gabr et al (1976) in his preliminary study showed an important association between chronic urticaria and intestinal parasites.

In urticaria pigmentosa, wheals occur in areas of trauma to the cutaneous benign mast cells tumours which characterize this disease. These pigmented macules or papules are seen most often in childhood, and the diagnosis is confirmed, if rubbing the lesions which produce urtication (Darier’s sign).

FOOD ALLERGY

Dees (1959) reported incidence of food allergy in children as 3%.

Fries (1959) after his study concluded that incidence of food allergy decreased with the advancing age.

According to Golbert (1969) food allergy cause a variety of cutaneous, gastrointestinal and respiratory manifestations; urticaria and angioedema are the most common.

The clinical manifestation of food allergy usually result from type I hypersensitivity (Golbert, 1970).

Chua et al (1976) have shown that positive cutaneous tests neither establish nor confirm a definite diagnosis of clinically significant food allergy.
May (1976) also has similar opinion.
Both Chua et al and May demonstrated presence of reaginic antibodies in patients who had negative prick test.

EOSINOPHILIA AND ALLERGY

Eosinophil leukocyte is characterised by the presence of large coarse cytoplasmic granules of prominent red colour (Romanowsky staining method) and by a nucleus which has one or two segments.

Apart from phagocytic and cytotoxic activity eosinophils are attracted to the site of immediate hypersensitivity reaction and has the unique potential to modify and regulate the reaction.

Eosinophils normally account for fewer than 5% of circulating leukocytes. Eosinophils counts more than 5% in peripheral smear or 250% cells per cmm is considered elevated. Blood eosinophils in the allergic disorder does not exceeds 15-20%, but may occasionally be high as 33% in allergic conditions.

In asthma eosinophils play dual part in protecting the patient from the effects of mast cell vasoactive mediators and simultaneously damaging the bronchial mucosa.

Bray and Smith (1931) found that eosinophilia was predominantly associated with allergic disorders.

Eosinophilia was reported in majority of cases of bronchial asthma by Lowell et al (1967).
Sehgal et al (1973) in a study of 158 patients with urticaria and angioedema reported eosinophil count of more than 10% in 26.6% cases.

Gupta et al (1975) observed eosinophilia irrespective of the type of asthma in their study.

Agrawal et al (1979) also reported significantly high absolute eosinophil count (917.71±618.9) in cases of bronchial asthma, compared to controls (231.4±105.4).

Lukza et al (1982) on the other hand found eosinopenia in cases of acute asthma and eosinophilia in cases of chronic and stable asthma.

Eosinophilia in varying degree, 10 to 40% was also reported by Akharya (1983) in their study of childhood asthma.

In addition to atopic illnesses and parasitic infections many infectious, inflammatory, neoplastic and even immunodeficiency problems are associated with profound alteration in circulating eosinophils, thus limiting the diagnostic significance of eosinophilia.

**PARASITES AND ALLERGY**

Jarrett (1972) have suggested that potentiation as a result of parasitic infestation, could increase the severity of an individuals allergy by elevating specific IgE level to undesired allergens, such as ragweed pollen etc.

Pasricha (1972) underlook the study to ascertain how far gastrointestinal parasites were responsible for
producing urticaria. Incidence of parasites in urticaria was not different from that in other dermatological diseases (61.5% and 72% respectively). Twenty five patients of urticaria harbouring gastrointestinal parasites were treated but only in two patients was the elimination of E. histolytica associated with a significant decrease in the intensity of urticaria.

Habte Gabr et al (1976) in their preliminary study showed an important association between chronic urticaria and intestinal parasites. Urticaria in 11 out of 14 patients had direct relationship to intestinal parasites, particularly Ascaris and was cured when the specific parasites were eliminated with anti-helminthic drugs.

Pasricha et al (1979) again surveyed the causes of urticaria and found only 7(1.4%) cases in whom elimination of parasites had resulted in relief from urticaria. Their studies however, did not account for urticaria caused by allergy to Larva of Ascaris and Hook worm as they traversed tissues before reaching gastrointestinal tract. Such cases of urticaria were likely to be of short duration as once larvae reached gastro-intestinal tract and matured, the antigenic stimulation would disappear, as opined by authors.

Veronesi et al (1982) established a relationship between intestinal giardiasis and urticaria. They found in their study of 50 patients of chronic urticaria,
giardia in stool and all of them improved with metronidazole, which was more than coincidental.

Hamriek et al (1983) also reported cases of urticaria caused by giardial infestation. They reported that urticaria could occur after massive absorption of antigen following the death of parasite.

Twarog (1983) opined that parasitic infestations should be considered in individuals having urticaria specially in those who came from an endemic area, had peripheral eosinophilia and who had elevated IgE.

IMMUNOTHERAPY

The concept of immunotherapy, desensitization or hyposensitization was first defined by Bostock (1819) which was later employed in the actual treatment by Noon (1911). IgE mediated allergic diseases are unique in that the sublethal parenteral administration of antigen, that is responsible for the disease, may render the patient specifically tolerant to that antigen as long as antigen is administered.

In one of the earliest controlled trials of immunotherapy (Brunn, 1949), 78% of the patients treated with house dust extract improved or remained free from symptoms compared with 22% of the control group, who did not receive immunotherapy.
Frankland and Augustin (1954) reported that 94% of their patients who received immunotherapy for allergic rhinitis and asthma had improvement in their symptoms.

Mc Allen (1961) found that house dust extract by injection was ineffective, while treatment by inhalation of an aerosol of house dust extract gave good though short lived results.

Smith (1971) demonstrated the role of immunotherapy in asthma, induced by house dust.

Aas (1971) found that 87% of 52 asthmatic children with house dust reactivity had a significant reduction in bronchial reactivity after treatment with house dust immunotherapy.

Though many studies have shown beneficial effects of immunotherapy some workers have reported the other way. Bruce et al (1977) treated a group of patients of allergic asthma (sensitive to ragweed) and there was no improvement in symptoms after immunotherapy. Causes of failure were attributed to improper detection of antigen, failure to include other antigen to which patients were sensitive or low dosage of antigen given.

A study to compare atopic patients who had received immunotherapy for 5 years with a group of atopic patients who had not received immunotherapy showed that there was no increase in the incidence of autoimmunity, collagen disorders, or lymphoproliferative
disorders in the treated group (Levinson et al, 1978).

Phanuphak and Kohler (1980) described 6 of 20 consecutive patients with polyarteritis nodosa in whom the onset of the vasculitis symptoms coincided with immunotherapy (within 6 months in 5/6) for presumptive atopic respiratory disease and vasculitis persisted despite discontinuation of immunotherapy. In 3/6 of the patients the respiratory symptoms (for which immunotherapy was given) were present for less than 5 months, suggesting that the symptoms were present or occurred during the prodrome of polyarteritis. So, they suggested not to initiate immunotherapy in any patient until at least one year after the onset of allergic respiratory illness.

While immunotherapy is carried out for all types of allergic disorders, immunotherapy is not recommended for treatment of food allergy. In case of food allergy, dietary exclusion of food is the treatment of choice.