REVIEW OF LITERATURE

During the past two decades, few areas of medicine have experienced as dramatic a change in the rationale for therapy from pervasive empirism to a substantive degree of rational therapy. Allergy and clinical immunology is one of them. Basic immunological principles and mechanisms infact provide clues for the diagnosis and management of allergic diseases. Immune system takes into account those mechanisms which confer specific immunity. However, other nonspecific defense mechanisms like mucociliary epithelium of respiratory tract or proteolytic enzymes of external secretions, also exist in the body, which help to protect body.

Specific immunity implies the acquisition of a biologic response in which circulating antibodies or lymphocytes interact with a unique molecular, or a very restricted range of molecular configurations, presented to them. The molecules that elicit the immune response are called antigen which usually are high molecular weight proteins, carbohydrates or nuclic acids. Out of these, those that elicit an allergic or hypersensitivity response are called allergens.

ONTOGENY OF IMMUNE SYSTEM

The immune system arises from developing lymphoid tissue during embryogenesis. The lymphoid organs are
divided into two categories - central and peripheral. In humans the central lymphoid organ is the thymus. It gives rise to two major populations of lymphocytes mediating specific immunity.

There are B cells (Bursadependent) which are involved in humoral or antibody mediated immunity and T cells (Thymus dependent) involved in cell mediated immunity.

Thymus is rich in T cells, arising from a common lymphoid stem cell migrating to the thymus (Bryant, 1974). In thymus their differentiation is stimulated by a humoral factor produced by thymic epithelium, termed as thymopoietin or thymosin (Goldstein, Hooper et al, 1974; Wara et al, 1975 and Scheinberg et al, 1976).

T cells migrate from the thymus by way of the blood stream and lymphatics to populate the peripheral lymphoid organs i.e. the lymph nodes, spleen, bone marrow, tonsils and gut associated lymphoid system (Hall, 1974).

The division of lymphocytes into T and B cells was first described in chicken (Cooper, Peterson et al; Motica, 1966).

B cell precursors are demonstrable in the mammalian fetal liver and in adult bone marrow (Gathings wer, Lawton et al, 1977). Migration of B cells to the peripheral lymphoid organs also occur (Pearl, Vogler, Okos et al, 1978).
A third lymphoid cell evolving from the central stem cell line during this period is the monocyte or in it's mature form macrophage. Over past several years it has been recognised that interaction of macrophages with T and B cells is important in the initiation of the immune response and it's regulation (Pierce, Kapp, 1978).

HUMORAL IMMUNITY

Stimulation of production of specific antibodies depends upon the nature of antigen antibody activity in humans resides in five major classes of globulins. These immunoglobulins classes are termed IgM, IgA, IgD, IgE and IgG. 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, presence of T cells is required (Katz, Benacessaf, 1972). This subpopulation of T cells is known as HELPER T CELLS (Friedman, 1975; Graves, 1973). In contrast to the majority which are T dependent antigens, there are few antigens which do not require mediation by T cells. These are called as T independent antigens (Moller, 1973). Along with interaction of B and T lymphocytes, macrophages play a vital role. Initially antigenic proteins bind to macrophage before their recognition by T lymphocytes (Basten, Mitchell, 1976).

Macrophages 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 is called Ia or immune response associated, presumably coded for by a corresponding Ir or immune response gene. The combination of processed antigen and Ia is then presented to T cell for immune recognition and stimulation of T cell to helper activity or effector activity (Benacessaf B and Germain RN).

The nature of receptor on the T cell surface which recognize specific antigen is still open to the discussion (Saligmann M, Preud Homme JL et al). In contrast, B lymphocytes have readily identifiable IgD and IgM monomer present on their cell membrane (Saligmann N et al, Franklin EC, 1978).

REGULATION OF ANTIBODY SYNTHESIS

It is known that following interaction of macrophage, B lymphocytes undergo blastogenesis and are transformed into a mature plasma cells, which synthesize immunoglobulin. Many regulatory mechanisms, however, operate over this.

IgM - B cells are suppressed by circulating IgG antibody directed against the same antigenic specificity (Sercurz, Williamson and Fox, 1974). Furthermore suppressor T cells exert a regulatory effect. There is growing evidence that yet another T cell population may exist, generating an opposing amplifier signal. Amplifier and suppressor T cells appear to generate complementary
effects to keep the degree of B cell activity appropriate to antigenic stimulation (Benacessaf, 1978). Macrophages also exert modulatory influence on B cell biosynthesis mediated by elaboration of so called monokine which enhances antibody formation (Dimitrin and Fanci, 1978).

**IMMUNOGLOBULINS**

Following types of immunoglobulins exist.

**IgG**

This is the major protective antibody of intravascular compartment. It's concentration usually increases with repeated antigenic stimulation. It's molecular weight is 150,000 Dalton with a half life of 23.0 days. Adult serum concentration is 600-1800 mg/dl.

**IgM**

It is found in lesser concentration than IgG. This is earliest antibody produced in most primary immune response. It has a molecular weight of 900,000. It's serum concentration is 60-250 mg/dl.

**IgA**

It comprises about 20% of serum immunoglobulins. It's important role is as protective antibody of the external and internal secretion. It is present in large amounts in saliva, colostrum, lacrimal and nasal secretions. It has a molecular weight of 170,000 Daltons. It's serum concentration is 90-450 mg/dl.
**IgD**

It is found free in circulation in low concentration. It serves as an antigen receptor or recognition site on the uncommited B cell. It's molecular weight is 184,000. It's serum concentration is 0-14 mg/dl.

**IgE**

IgE has been shown to be the principal mediator of immediate (type I) hypersensitivity reactions (Norman, PS). IgE binds to tissue mast cells and basophils. This cell bound complex then causes degranulation of basophils on combining with allergen. With the result histamine and other mediators of type I reaction are released (Beaven MA). Its molecular weight is 190,000. It is present in lowest concentration (10-406 IU/ml). IgE concentrations are generally higher in the allergic population although there is considerable overlapping with nonatopics (Horburger, 1978).

**CELL MEDIATED IMMUNITY**

The parallel mechanism of immune recognition and immune regulation are analogous in humoral and cell mediated immunity (Parker CW). However, immune reaction in CMI (cell mediated immunity) is brought about by sensitized lymphocyte, rather than a free antibody molecule. The development of antigen specific T lymphocytes is dependent on interaction of macrophage and T cell. After antigen recognition a proliferative phase ensues, morphologically characterised by production of lymphoblasts
1. Memory T cells: These cells are fairly long lived and are important in maintaining immunologic memory of previously encountered antigens (Benner R, Von Odenarm A et al, 1977).

2. Suppressor T cells: Both immunoglobulin class specific and antigen specific suppressor T lymphocytes have role in antibody production. They have role in regulation of effector cell's response in CMI. They also establish tolerance to self antigen (Kapp JA, Pierce CW et al, 1968).

3. Amplifier T cells: They act in opposition to suppressor T cells in regulation of B cell activity. It is however, not clear that an analogous population is operative in regulation of CMI.

4. Effector T cells: They on contact with antigen create the molecular cellular and clinical manifestation of CMI reaction.

Macrophage which is not a T cell. Can also exert a regulatory effect on effector cell activity in CMI. This activity is different than it's role in initiation of antigen specific immune responsiveness. Effector T cells are induced to perform their functions by elaboration of soluble mediators called lymphokines (JJ Oppenheim), which are produced by antigen specific memory T cells upon contact with antigen.
5. Killer or K cells: These cells bring about lysis. They are in fact the sensitized effector T lymphocytes. Binding of K cells to target cells is a pre-requisite for lysis.

**CLASSIFICATION OF HYPERSENSITIVITY REACTIONS**

Gell and Coomb classified hypersensitivity reactions. Several modifications however have been proposed to the Gell and Coomb classification system (Sell, 1975). Many immunological processes incorporate more than one type of hypersensitivity reaction.

1. **Type I (Anaphylactic) Reaction:**

   This type of reaction is also called immediate type hypersensitivity or reaginic hypersensitivity. Clinical condition as extrinsic bronchial asthma, allergic rhinitis, urticaria, food allergies and reaction to stinging insects and systemic anaphylaxis, all are mediated by this type of immune reaction. Immunoglobulins which mediate this reaction are called reagin. Ishizaka and Ishizaka (1970) have shown that IgE possess the classic characteristics of reagin. IgE does not cross placental barrier. This can freely circulate in blood or may remain bound to basophils and/or mast cells. Anaphylactic reaction is brought about by many mediators. Histamine, SRS-A, serotonin, eosinophilic chemotactic factor of anaphylaxis, platelet activating factor, prostaglandin are all mediators that potentially can give rise to hypersensitivity
capillary permeability and contraction of smooth muscles.

**Type II (Cytotoxic) Reaction**

These reactions are also termed as complement dependent cytotoxicity. Complement system is also required to mediate type III or toxic complex reaction along with this type.

In type II reaction this system works when cell bound antibodies combine with antigen and in type III reactions it works when cell bound antibody and antigen complex has settled down at the place of reaction. Complement system is composed of serum protein which when react in combination have the capacity to cause cell lysis.

Ehrlich and Bordet put the guidelines of events involved in cell lysis.

Complement system involves two major subsystems.

1. Classical pathway.
2. Alternate pathway.

In the activation of complement system there is:

1. Sequential activation of inactive precursors. (zymogenes).
2. Activation of increasing number of molecules in subsequent steps of the sequence (Cascade).
3. Amplification of propagation of inflammation by product of activation.

Type II reactions have two subgroups.
In one complement fixing antibody is directed against endogenous antigenic determinant of cell membranes, example - Transfusion reactions.

In second group the antigenic determinant is exogenously introduced and then binds to the cell membrane, example. Haemolytic disease of new born and neonatal thrombocytopenic purpura.

3. **Type III or Toxic Complex Reaction**

These reactions are also referred as immune complex hypersensitivity reactions. Clinical conditions that are mediated by toxic complex reaction include Arthus reaction, clinical serum sickness and certain glomerulonephritides. Complexes made of cell - antibody - antigen settle at the place of reaction, and through activation of complement system damage is produced.

4. **Type IV or Cellular Hypersensitivity**

This is also called delayed hypersensitivity as a delay of 24 to 72 hours occurs in the initiation of reaction. Delayed hypersensitivity is not mediated by circulating antibodies, but is mediated by antigen specific sensitized lymphocytes. Tuberculin hypersensitivity contact dermatitis, allograft rejection, Graft versus host disease as a sequele to bone marrow transplantation are conditions which involve type III reaction.

Richet and Porter had described the development of anaphylaxis in dogs. In 1922 Prausnitz and Kustner
described the transfer of immediate hypersensitivity from an affected individual to a normal individual by serum, and the test employed for the detection of presence of this type of antibodies was termed as P-K test.

Medical evaluation for atopic diseases like allergic asthma, allergic rhinitis, urticaria traditionally has consisted of three parts:

1. History.
2. Physical examination and
3. Skin testing with appropriate allergen.

Different techniques of performing allergy skin test are well known (Mangi RJ) and variability between commercial allergen also is well documented (Ford DW, et al and Tunginger JW).

There are other variable as well which also affect the skin test interpretation. They are:
2. Instrument used to apply test (Sheldon JW et al).
3. Criteria for grading result of skin test (Patterson R).
4. Time of day (Lee RE et al).
5. Area of body where test is applied (Voorhorst R.).
6. Subjective evaluation of skin test reactivity by different personnel (Aas K.).

Skin prick test for allergy detection involves allergen induced wheel and erythema response which was firstly described by Blackley.
In 1954 Herzheimer et al studied the evaluation of skin test in respiratory allergy.

Holman et al studied skin test and bronchial challenge test correlation and concluded that it is the skin test with provides important information when considering immunotherapy.

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

From time to time the safety, cost and effectiveness of skin allergy test has been studied. When compared to skin test other tests are expensive and less sensitive (Adkinson NF).

Coca and Grove did extensive studies of the skin sensitivity factor from sera of patients with ragweed hay fever. Gleich and co-workers have been able to define the natural rise and fall in ragweed specific IgE over a period of one year. Ishizaka and Ishizaka using RAST technology had made observation that there is rise in IgE after a pollen season.

Although RAST and other IgE measuring technology have added to the knowledge, these tests at present do not replace simple skin testing with the allergen, moreover skin test provides important information when treatment is being planned (Gleich et al).

Most testing is dependent on the production of an allergic reaction by the intentional exposure of the
are used in clinical practice.

With the Scratch test antigen is applied to a superficial scratch that penetrates the outer cornified area of skin. In prick test skin is pricked by a needle through a drop of antigen solution. Intercutaneous test is performed by injecting a small amount of antigen in the superficial layers of skin. The antigens used may vary because of the prevalence of particular antigens in a particular geographical location. Results of SPT are often compared with those obtained by other methods.

Juhlin and Dannfelt have failed to obtain a positive bronchial response to any antigen when the skin tests have been negative on the other hand Colldahl in his study has found positive bronchial reaction in patients who had negative skin test.

SPECTRUM OF ILLNESS

1. Allergic Rhinitis

Seasonal allergic rhinitis is a specific allergic reaction of the nasal mucosa principally to pollens, characterised mainly by watery rhinorrhea, nasal congestion, sneezing, itching of eyes, nose and throat though there is no fever essentially still this condition is also referred as Hay fever. Though its incidence is greater among children and young adults, no age, however, is exempt. Cooke and Vandeneveer showed the role of heredity in etiology. Tennensawm (1970) also endorsed their findings.
Phillips has shown that individual requires two or more seasons of exposure before exhibiting clinical manifestation of disease.

Smith reported that 80% of patients develop their symptoms before the age of 30 years. Cell bound IgE antibodies in the response of antigenic stimulation, cause release of mediators of immune reaction and bring about manifestations of disease (Kaliner M, Wasserman SI and Austin KF, 1973).

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 climate changes.

Nasal provocation testing to detect the condition with suspected allergens is of research value as there are difficulties and so it's clinical usefulness is limited (Solomer and Mclean, 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.

Some patients develop shortness of breath due to allergic tracheobronchitis. This may be a warning signal of possible development of allergic asthma. The characteristic of symptom complex is that it appears at a certain time of year and its periodicity or frequency.
Mygind and Lowenstein (1982) have shown that atopic skin test positive rate is 35% in healthy population. Aas has proved that immediate skin tests for some allergens are equally reliable as RAST.

**Perennial (Nonseasonal) Allergic Rhinitis:**

In this condition there is intermittent or continuous nasal symptoms due to allergic reaction without seasonal variation. There is usually a chronic antigenic challenge resulting in recurring almost continuous symptoms. Major perennial allergens include house dust, feathers, mold, animal denders. This may be due to occupational allergens, example, in flour industry workers (studied by Schwartz M), Detergent workers (studied by New house M) and wood workers (studied by Sosman AJ) diseases occur due to hypersensitivity to these things.

Alteration of normal physiology and symptom complex of this condition are similar to seasonal allergic rhinitis but are less severe and more constant.

**Vasomotor Rhinitis**

It is associated with an altered vasomotor control resulting in the development of chronic nasal congestion. This is nonimmunologic, non infectious. many nonspecific stimuli act on the autonomic nerves resulting in reflex changes in the nasal mucosa.

Holmes, Goodell and co-workers have shown that emotional stimuli trigger nasal obstruction and rhinorrhea.
may induce similar nasal changes. Most patients with this condition show no reaction to skin test, but a small proportion may show a positive result which is incidental and does not correlate with clinical history.

**Infectious Rhinitis**

In this form there is fever and malaise along with local symptoms. Discharge is purulent, each attack may last for 1-2 weeks.

**Hyperplastic Rhinitis**

In this condition purulent sinusitis superimposes upon allergic rhinitis, there is marked mucosal oedema. Kern and Schenic have shown that nasal polyps occur in uncontrolled allergic rhinitis.

**Difference between Allergic and Nonallergic (vasomotor) Rhinitis**

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Allergic</th>
<th>Vasomotor</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Seasonal variation</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>2. Nasal, ocular, palatal itching</td>
<td>Present</td>
<td>Rarely</td>
</tr>
<tr>
<td>3. Rhinorrhoea</td>
<td>Watery</td>
<td>Mucoid</td>
</tr>
<tr>
<td>4. Pale nasal mucosa</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>5. Collateral allergy</td>
<td>Common</td>
<td>Unusual</td>
</tr>
<tr>
<td>6. Nasal polyp</td>
<td>Occasional</td>
<td>Occasional</td>
</tr>
<tr>
<td>7. Family history of allergy</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>8. Nasal secretion eosinophilic smear</td>
<td>Positive</td>
<td>Rarely positive</td>
</tr>
<tr>
<td>9. Skin test reactivity</td>
<td>Almost always positive</td>
<td>Negative</td>
</tr>
</tbody>
</table>
2. **Allergic Asthma**

Word 'Asthma' is derived from a Greek word meaning short drawn breath. There is no universally accepted definition of Asthma. It may be regarded as diffuse obstructive lung disease with hyperreactivity 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. Irritability or hyper-reactivity of airways is manifested as broncho-constriction following exercise, natural exposure to strong odour, irritant fumes, tobacco, smoke, cold air, or intentional exposures to parasympathomimetic agents. Polygenic or multifactorial determinants control the inheritance of asthma. Lability of broncho-constriction with exercise has been found concordant in identical twins but not in dizygotic twins. Bronchial lability in response to exercise testing also has been demonstrated in healthy relatives of asthmatic children.

**Etiology**

Asthma is a complex disorder involving immunologic, autonomic, biochemical, infective, endocrinal and psychologic factors, in varying degree in different individuals. Neural and humoral factors govern the diameter of airways. Neural broncho-constrictor activity is mediated through the cholinergic portions of autonomic nervous system. Vocal sensory ending initiates end stimulate bronchial smooth muscle contraction. On the
neural bronchodilator side a non adrenergic inhibitory system is found like that of ganglionic cell of myenteric plexus. Humoral factors of bronchodilation include catecholamines which act on beta adrenergic receptor to produce relaxation of bronchial smooth muscle. When humoral substances such as histamine and SRS A are released through immunologically mediated reaction, they produce broncho constriction either by direct action on smooth muscle or stimulation by vegal sensory receptors.

Szentivanji's theory considers asthma, to be due essentially to abnormal beta adrenergic receptor adenylate cyclase function with decreased adrenergic responsiveness. The recent report of decrease beta adrenergic receptor on leucocyte of nonadrenergic drug treated asthmatics may provide the morphological basis for the observed hyporesponsiveness to beta agonist. Alternatively, increased cholinergic activity in the airway has been proposed as fundamental defect in asthma, perhaps due to some intrinsic or acquired abnormality in irritant receptors which have been seen to lower threshold for response to stimulation. In individual patient a number of factors generally contribute in varying degree to the activity of asthmatic process.

Clinical Manifestations

The onset of attack is usually acute through it may be insidious. There is cough which sounds light and is nonproductive early in the course. Wheezing tachypnoea and
prolonged expiration are present. There may be use of accessory muscles of respiration and hyperinflation of chest. Abdominal pain may be present depending upon the severity and duration of illness. Recurrent episodes and precipitation of attack on exercise is characteristic.

Rackman (1963) divided asthma into extrinsic asthma which is caused by allergen or external factors and intrinsic asthma caused by non allergic factors.

Differences between two types are:

<table>
<thead>
<tr>
<th>Symptoms</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>Mucous</td>
<td>Clear and foamy</td>
<td>Thick and white or colourless.</td>
</tr>
<tr>
<td>Atopy</td>
<td>+ve</td>
<td>Absent</td>
</tr>
<tr>
<td>Skin test</td>
<td>+ve</td>
<td>Negative</td>
</tr>
<tr>
<td>Serum IgE</td>
<td>High</td>
<td>Normal</td>
</tr>
<tr>
<td>Response to therapy</td>
<td>Good response to immunotherapy and bronchodilators.</td>
<td>Poor response to therapy</td>
</tr>
</tbody>
</table>

Clinically asthma can further be described as

spamotic - If isolated attack occurs with longer symptoms free intervals.

Continuous - When some amount of wheezing is present almost everyday.
Intractable: When symptoms are constant and refractory to treatment.

Status asthmaticus: When little or no response is obtained to bronchodilators as patients respiratory metabolism is greatly imbalanced.

There is a special category of nonantigenic asthma. This is induced by the ingestion of aspirin, as described by Samter and Beer. Skin tests to aspirin are always negative in these patients.

3. Urticaria

It consists of raised, erythematous, skin lesions which are marked by pruritis. Angioedema is characterized by asymmetrical swelling of tissue. This is like urticaria but involves deeper tissue. Urticaria and angioedema may occur together.

Mathews concluded that nearly 20% population at some time in life suffers some form of urticaria. Acute urticaria persists less than 6 weeks while episodes which last more than 6-8 weeks are referred as chronic urticaria. Pathogenesis is being mediated by histamine release.

Triple response observed by Lewis, is consist of erythema due to capillary and vascular dilatation, oedema due to increased capillary permeability and flare due to axon reflex. Intercutaneous injection of histamine inflicts similar type of response along with pruritis implicating that histamine mediates the urticarial response.
Urticaria occurs due to IgE mediated immediate hypersensitivity induced by antigen and being brought about by histamine release from mast cell via complement eosinophil chemotactic factor and platelet activating factor. Direct histamine release occurs with some drugs and chemicals. Plasma Kinin system may play a role in causation of urticaria by producing bradykinin which is known to increase capillary permeability. This system is activated by negatively charged surfaces, collagen vascular basement membrane or endotoxin. Fever, heat, alcohol intake, exercise, emotional stress, premenstrual or postmenstrual status, hyperthyroidism, adrenergic and cholinergic agents modulate mediator release from mast cells and basophil and may play a role in causation of urticaria.

Classification of Urticaria

Following are the types of urticaria.

1. Dermographism.
2. Physical urticaria.
3. Hereditary urticaria.
4. Papular urticaria.
5. Urticaria pigmentosa.
6. Miscellaneous (caused by drugs, food, systemic vasculitis, infections, serum sickness, psychogenic cause insect bite and transfusion reaction).
4. **Food Allergy**

Dees reported incidence of this in children as 3%. Fries after his study concluded that incidence decreases with the advancing age. According to Golberg, food allergy causes variety of cutaneous, gastroenteritisal and respiratory manifestations. Urticaria and angioedema is most common. The clinical manifestation of food allergy usually result from type I hypersensitivity (Golbert).

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 had similar opinion. Both Chua et al and May demonstrated presence of reaginic antibodies in patients who had negative prick test. According to other study skin tests were negative in only 24% of patients who had positive history of food allergy.

**ALLERGEN IMMUNOTHERAPY**

Immunotherapy refers to the treatment in which patient is given injections of antigenic material to which they are sensitive.

Freeman and Noon (1911) firstly treated grass pollen sensitive patients with injection of extract of grass pollen. They treated 18 patients who had sensitivity to grass pollen and 16 patients had beneficial effects.

Cook conducted similar studies. In his study 114 patients were treated with pollen immunization for ragweed allergy and nearly half of them had beneficial
effects.

Since 1949, many studies have been conducted using immunotherapy to the patients who had allergic disorders (Fontana, Holt et al, 1966). Lowel and Franklin (1965) conducted double blind study of the effectiveness of immunotherapy for ragweed hay fever. Melam, Pruzanbky and Patterson et al (1971) also showed beneficial effects of injection immunotherapy. Sadan, Rhyme and Mellits investigated immunotherapeutic response in pollinosis in children.

Frankland and Augustin have reported that 94% of their patients who received immunotherapy for asthma and rhinitis had improvement in their symptoms.

Brown (1949) conducted one of the initial studies concerning immunotherapy to house dust sensitive patients. He showed 78% of patients had improvement in their symptoms.

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

Taylor et al (1978) have shown improvement in symptoms in asthmatic patients sensitive to cat dander after treatment with a very potent cat pelt vaccine.

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

The safety of immunotherapy has also been challenged from time to time.

Kohler in his study found development of Arteritis in patients who were undergoing immunotherapy. Kohler and Phanupak have shown that 5 out of 19 patients treated by immunotherapy developed polyarteritis nodosa.

Levinson, Summers, Lawley et al (1978) compared a group of atopic patients receiving immunotherapy for five years with those who were not receiving any therapy. The treated group did not show an increased incidence of autoimmune collagen vascular or lymphoproliferative disease.

Lichenstein, Norman and Winhenwerder (1968) have shown that immunotherapy leads to an increase in IgG blocking antibody titres. These antibodies block histamine release by combining with antigen before it reacts with IgE antibodies fixed to mast cells. The rise in titre is dose dependent.

Starr and Weinstock (1970) have shown that higher titres result in less symptomatic patients. There is a decrease in sensitivity of leucocytes to histamine release to antigen following immunotherapy.
According to Sherman, Stull and Cooke there is a decline in serum IgE directed against specific antigens in patients receiving immunotherapy.

Levy (1971) found that there is also a decrease in the post season rise in IgE directed against specific antigens in patients receiving immunotherapy.

By immunotherapy IgE reduction is produced by:

1. Induction of suppressor mechanisms within the allergic individuals to reduce the production of IgE.

2. Induction of specific immunologic tolerance in IgE precursor B lymphocytes which are precursors cells of IgE producing plasma cells.

While immunotherapy is carried out for all sorts of allergic disorder, immunotherapy is not recommended for treatment of food allergy. If food allergy is present dietary exclusion of foods is the treatment of choice.
AIMS OF STUDY

1. To study the spectrum of various allergic disorders prevalent in the Bundelkhand region and confirm their allergic etiology.

2. To find out the prevalence of various allergens and which one is commonest.

3. To evaluate the effect of immunotherapy in the management of these disorders.