REVIEW OF LITERATURE
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Von Pirquet (1906) coined the word allergy to refer to 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.

Ellis (1983) defined allergic disorder as "adverse physiological reaction resulting from the interaction of antigen with humoral antibody and/or lymphoid cells". Bronchial asthma is one of the allergic disorders in which alteration in IgE, complement and eosinophils has been seen.

BRONCHIAL ASTHMA:

The term asthma is derived from the Greek word meaning "struggling for breath". There is no universally accepted definition of asthma. It may be regarded as a chronic inflammatory disorder of the airways in which many cells play a role, including mast cells and eosinophils.

Bruce (1958) observed that nearly 50 percent patients of asthma had a family history of allergy.
Vishwanath (1964) defined bronchial asthma as a syndrome that is characterised by attack of expiratory dyspnoea not attributable to disease of the heart or lung. The smooth muscle in the bronchi and bronchiols exhibit spasm, edema and exudation following exercise, natural exposure to strong odours, irritant fumes, tobacco, smoke, cold air, and intentional exposure to parasympathomimetic agents.

Ellis (1983) observed that eighty to ninety percent of asthmatic children had their first attack before the age of five years. Prior to puberty about twice as many boys as girls were affected. Thereafter, sex incidence was equal.

**Pathophysiology:**

Whilst the bronchial hyper-reactivity results in bronchospasm with hypertrophy and hyperplasia of smooth muscles, the other essential ingredient of airflow limitation is an inflammatory reaction. In patients dying from asthma small airways are plugged with thick, viscid mucus, often forming casts. There is hyperplasia of goblet cells and basement membrane, sloughing of epithelium and submucosal infiltration with eosinophils, lymphocytes, mast cells and neutrophils (Warner 1984).
The obstruction produces increased airway resistance, which lowers the force of expiratory volume, and flow rates; causes premature closure of airways, hyperinflation of lungs; brings about increased work of breathing, change in elastic properties and frequency dependent behaviour of lung. Although airway obstruction is diffuse, it is typically nonuniform, from one part of the lung to another. This results in ill perfusion of inadequately ventilated portion of lung and leads to abnormalities of blood gases (Behrman and Vaughan 1987).

ETIOLOGY:

Asthma is a complex disorder involving biochemical autonomic, immunologic, infectious, endocrine and psychological factors. The control of the diameter of airways may be considered a balance of neural and humoral forces. Neural broncho-constrictor activity is mediated through the cholinergic portions of autonomic nervous system. Vagal sensory ending in airway epithelium, termed cough or irritant receptors, depending upon their location, initiate the afferent limb of reflex are which at the efferent end stimulate bronchial smooth muscle contraction. Humoral factor of broncho-dialation includes the endogenous
catecholamines which act on beta adrenergic receptors to produce relaxation in bronchial smooth muscles. In an individual patient a number of factors generally contribute, in varying degree, to the activity of asthmatic process (Behrman and Kliegman 1990).

**CLINICAL MANIFESTATION:**

Rackeman (1964) suggested separating asthma into extrinsic atopic asthma caused by allergens or external factor and intrinsic or nonatopic asthma caused by non-allergen factors.

Asthma presents with recurrent episodes of non-productive cough, chest tightness, dyspnea with prolonged expiration, tachypnea, wheezing, cyanosis, tachycardia and use of accessory muscles of respiration. Pain in abdomen may be present due to strenuous use of abdominal muscles and diaphragm. A barrel chest deformity is a sign of chronic, unremitting airway obstruction of severe asthma (Behrman and Kliegman 1990).

Warner et al (1992) classified asthma on the basis of severity and airflow obstruction as follow:
<table>
<thead>
<tr>
<th>ASTHMA SEVERITY</th>
<th>CLINICAL FEATURES</th>
<th>LUNG FUNCTION</th>
<th>REGULAR MEDICATION USUALLY REQUIRED TO MAINTAIN CONTROL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Intermittent, brief symptoms ≤2 times a week.</td>
<td>PEF 780% predicted at baseline.</td>
<td>Intermittent inhaled short acting beta₂ agonist (taken as needed) only.</td>
</tr>
<tr>
<td></td>
<td>Nocturnal asthma symptoms ≤2 times a month.</td>
<td>PEF variability ≤20%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>A symptomatic between exacerbations</td>
<td>PEF normal after broncho dilator</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>Exacerbations 71-2 times a week</td>
<td>PEF 60-80% predicted at baseline.</td>
<td>Daily inhaled anti-inflammatory agent.</td>
</tr>
<tr>
<td></td>
<td>Nocturnal asthma symptoms 72 times a month.</td>
<td>PEF variability 20-30%</td>
<td>Possibly a daily long acting bronchodilator, especially for nocturnal symptoms.</td>
</tr>
<tr>
<td></td>
<td>Symptoms requiring inhaled beta₂ agonist bronchodilator almost daily.</td>
<td>PEF normal after bronchodilator.</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>Frequent exacerbations</td>
<td>PEF 50% predicted at baseline.</td>
<td>Daily inhaled anti-inflammatory agent at high doses.</td>
</tr>
<tr>
<td></td>
<td>Continuous symptoms</td>
<td>PEF variability 7/30%</td>
<td>Daily long acting bronchodilator especially for nocturnal symptoms.</td>
</tr>
<tr>
<td></td>
<td>Frequent nocturnal asthma symptoms</td>
<td></td>
<td>Frequent use of systemic corticosteroids.</td>
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<tr>
<td></td>
<td>Physical activities limited by asthma</td>
<td>PEF below normal despite optimal therapy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hospitalization for asthma in previous years.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Previous life threatening exacerbation.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
NOTE: The characteristics noted in this table are general and the characteristics may overlap because asthma is highly variable. Furthermore, an individual's classification may change over time.

One or more features may be present to be assigned a grade of severity.

ALLERGY IN ASTHMA:

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

Johnson (1967) found that 63% of patients with allergic asthma had raised IgE level in serum, while it was only 5% in those with non allergic asthma.

Robinson (1973) suggested that asthmatic paroxysm was triggered by the hypersensitivity reaction or by mental stress. Allergy was always a basic factor of an asthmatic paroxysm, as opined by the author.

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

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

Frick and Mills (1979) observed a role of viral infections in the allergic sensitization process. They studied 16 children including 2 cases, who had history of
atopy. Out of 16 children 11 developed clinical allergy and 5 developed asthma after an attack of respiratory viral infection.

Raihi et al (1990) showed an agreement existing between the history of asthma and allergy to house dust: bronchial challenge to whole house dust was positive. All allergic patients had significant bronchoconstriction, whereas, no reaction could be elicited in the non-allergic group.

**IMMUNOLOGIC SYSTEM IN BRONCHIAL ASTHMA:**

Immunologic system is the part of host defence, its primary function is to protect against invasion by infectious agent. The costs of this protection are allergy and auto-immunity. There are four major limbs of immune system: T lymphocyte, B lymphocyte, phagocyte and complement. At least twice the population of lymphocytes are involved in most of immune responses (Claman et al 1966, Devis et al 1967, Millar and Michel 1968).

Antigen induced asthma is representative of a type-I hypersensitivity reaction. This specific response originates in the homocytotropic or reaginic antibody (immunoglobulins that can attack mast cells or basophils). But clinical significance is not clear in so-called short term sensitizing antibody (Metcalf et al 1981).
In 1982, Oshea observed that IgG may act like a reagenic antibody.

Anderson (1984) suggested that non-immunologic mechanism also played a role in the pathogenesis of atopic disease named anaphylactoid reaction (Non IgE mediated anaphylaxis like reaction).

Type-I hypersensitivity reaction is initiated by allergen exposure, B cell stimulation and production of IgE. IgE binds with specific receptors which are present on mast cell and basophil surfaces. On repeated challenge by specific antigen the second stage of reaction comes into play with binding of antigen to the surface bound IgE. When an antigen bridges at least two IgE molecules, the cell is activated. The activated mast cells can then secrete mediators, that exist preformed in its granules. This process known as degranulation, releases histamine, leukotrienes, eosinophil chemotactic factor or anaphylaxis and prostaglandings that cause the symptoms of type-I hypersensitivity (Behrman and Vaughan 1987).
ROLE OF INFECTION IN BRONCHIAL ASTHMA:

The role played by infection in childhood asthma can only be estimated by empirical and indirect means. Even today, no one seems to doubt that respiratory infection is the most important triggering factor in bronchial asthma. However, thorough investigation of 400 children referred from pediatrician under the diagnosis of pure infectious asthma showed that 373 (95%) of them had other precipitating causes (Aask et al 1963).

Inflammatory reactions in the bronchi cause obstruction due to thickening of bronchial mucosa, increased secretion and impaired ciliary activity with long lasting undesirable changes in ventilation dynamics (Hall et al 1976).

Viral infection that produce airway epithelial damage, airway damage may expose the irritable airway receptors to react more easily to inhaled and other irritants (Empey et al 1976).

Respiratory infection may result in undesirable change in beta adrenergic tone and responsiveness to adrenergic stimulation (Busse et al 1977).
Infections with common bacteria and viruses do not influence the total serum IgE level. Serum IgE was reported to be elevated in an infant with para-influenza virus infection but did not appear to be an acute phase reactant (Sieber et al 1977).

There are several reasons why infection may precipitate bronchial asthma and particularly so in childhood, when the bronchial lumen is narrow. The mucosal lining becomes more radially swollen following infections than is the case in later life. In other words, infectious asthma may be considered an expression of the characteristic bronchial hyperactivity to a number of different stimuli, rather than immunological hypersensitivity (Flaherty 1977).

IgE IN BRONCHIAL ASTHMA:

In 1967, Ishizaka et al discovered that a reaginic skin sensitizing antibody belongs to a unique class of immunoglobulins which they called IgE.

Johansson et al (1970) found raised IgE level in bronchial asthma, atopic dermatitis and allergic rhinitis. He also noted that IgE level varied with age but not with sex.
Toda (1975) observed IgE level approximately 500,000 µg/kg of body weight and intravascular half life to be 2-3 days. The synthesis rate was 2.3 µg/kg/day. Thus, one third of the total body pool of IgE was replaced every day. Only 1% of the total IgE was cell bound.

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

Beavan (1976) reported that IgE binds to tissue mast cells and basophils. This cell bound complex then caused degranulation of basophils on combining with antigen (allergen) with the result that histamine and other mediators were released.

Homburger (1978) suggested that IgE concentration was generally raised in the allergic patients.

The IgE myeloma protein has a molecular weight of 1,90,000 with a sedimentation coefficient of 8s. It is a glycoproteins and like all immunoglobulins, it has a 4 chain structure, with two light and two heavy chains. The heavy chains like those of IgM, contain five domains which carry unique antigenic specifications, termed the epsilon determinants. It is those unique
antigenic structures which determine the class
specificity of this protein. No other immunoglobulin
heavy chain has epsilon antigenic determinants. The
Fc fragment of immunoglobulin is responsible for the
protein's ability to fuse to receptors on mast cells
and basophils (Zeiss 1980).

GENETICS OF IgE:

The heritability of atopic disease was recognized
as early as 1872. In most family studies a positive
family history has been reported in 50-75% cases.

Adkinson (1920) proposed a recessive mechanism
for inheritance of atopy but Spair and Cooke (1924),
Bucher and Keeler (1930), favoured a simple Mendelian
dominant inheritance.

Bray (1934) suggested a bimodal distribution of
the onset of atopic disease.

Opree et al (1972) agreed with the observations
that atopy was transmitted by two alleles at a single
locus and that predisposition to atopy and synthesis of
IgE were under identical genetic control.

Marsh (1974) analysed data from allergic families
in terms of bimodal distribution and suggested recessive
inheritance for high IgE levels.
Leung et al (1985) reported that T lymphocytes played an important role in the isotype specific regulations of the human IgE response.

**DEVELOPMENT OF SERUM IgE LEVELS:**

Johansson (1968) while reporting serum IgE levels in infants and children showed very low levels, compared to those of adults. Author found mean cord serum level of IgE to be 36 ng/ml (15% of adult). There was no correlation between the mean IgE level in the serum of newborns and their respective mothers. A gradual increase in the IgE level was found during childhood up to a mean level of 248 ng/ml in healthy adults, although the distribution was rather wide 61.4-1000 ng/ml (about 95% confidence limits), as the author wrote.

Berg et al (1969) reported serum IgE level in 132 healthy children who did not have any atopic disease. They also found a gradual increase in the mean IgE level from 137 ng/ml in the age group of 2-2½ years to 330 ng/ml in age group of 13-15 years.

In a longitudinal study of serum IgE level (Çrgel et al 1975), 34 infants (from atopic and non atopic families) were followed for full one year. Neonatal levels ranged from 0-10 units/ml. The 50th percentile level increased from 2.2 units/ml at 2 weeks of age to
3.8 units/ml at 6 months of age and 9.8 units/ml at 9 months of age. Half of the cases in the study group, who maintained serum IgE level below 10 units/ml, included a high proportion of infants from atopic families. The basal serum IgE level of individual adults was relatively stable over periods of 0.5 to 5.5 years.

Ishizaka et al. (1978) observed minimal concentration (0.25 ng/ml) of IgE antibody necessary to produce a positive Frausnitz-Kaustner (PK) reaction in man.

SERUM IgE LEVELS IN BRONCHIAL ASTHMA:

Johansson et al. (1967 & 68) measured serum IgE levels by radio-immunosorbent assay (RISA) in 38 patients of asthmatic bronchitis after dividing them into allergic and non-allergic groups on the basis of skin and provocation test and on clinical grounds. Authors found significantly raised serum IgE level in 63% patients with allergic asthma. Compared to this only 5% of patients with non allergic asthma had raised level of IgE. IgE level of 700 ng/ml was taken as the arbitrary limit of normal value by the author. Mean concentration of IgE was six times higher in group with allergic asthma (1589 ng/ml) than in the group with non
allergic asthma (275 ng/ml); while mean level in the control group was 330 ng/ml. However, there was no significant difference in IgE levels, between the patient treated with steroids or hypo-sensitization and those not so treated. Moreover, there was no age difference in the IgE level as reported by the authors. Authors, further reported that no difference existed between allergic and non-allergic patients with respect to the concentrations of IgE, IgD, IgA and IgM in the serum.

Berg et al (1969) observed high serum IgE levels in 90 percent of the cases of perennial asthma and 50 percent cases of seasonal asthma. Patients with perennial asthma had markedly higher IgE concentration than those, whose asthma was essentially seasonal, probably owing to repeated or continuous exposure of children with perennial asthma to allergens. In contrast to the earlier studies, these authors found that IgE concentration increased after desensitization. Higher IgE concentration was found in patients with a positive response to allergy test and the concentration was twice as high during the pollination season, than before.
Gleich et al (1970) observed high serum IgE level in allergic asthma, and found higher IgE level in the group of untreated patients when compared to the group treated by hypo-sensitization. The finding suggested that IgE could decrease after hypo-sensitization (Johansson's 1969).

Henderson et al (1971) counted 76 percent of patients with higher IgE level, among allergic asthma cases as compared to only 21 percent, such patient among idiopathic asthma group, while taking 540 ng/ml as the arbitrary limit of normality. Workers explained that raised IgE levels in idiopathic group could be due to hidden allergic factors or other factors causing elevated IgE levels.

Spitz et al (1972) measured serum IgE with the use of Rowe modification of the mancini technique and showed significantly raised levels in atopic (357 ng/ml) and questionable atopic (233 ng/ml) patients when compared to normal person (88 ng/ml). Higher levels were also related to eosinophilia.

Loeffler et al (1973) reported high IgE levels with extrinsic asthma.
Key et al (1974) found that in 93 asthmatics patients (70 adults and 23 children) serum IgE levels was significantly higher.

Saha et al (1975) studied immunoglobulins IgG, IgD, IgA, IgM and IgE in the sera obtained from 69 bronchial asthma patients who were graded objectively according to atopic score. Among other associated atopic diseases, they often had allergic rhinitis. Nearly 91 percent of these patients had elevated serum IgE levels and mean level of serum IgE was more than 3.5 times higher than that observed in the normal subjects. Moreover, as their atopic score increased, serum IgE level also got elevated and every patient with high atopic score, had elevated serum IgE levels, indicating the association of atopic state with serum IgE level. Authors also reported a significant correlation between the intensity of intradermal test and prausnitz kustner (PK) reaction with serum IgE level.

Gupta et al (1975) observed increased IgE level in 39 percent patients of bronchial asthma. The detection of hyperimmunoglobulinaemia E in six out of twelve patient with peripheral eosinophilia and one out of five with normal counts suggests an association of eosinophilia counts with IgE level.
Lin et al (1977) found elevated serum IgE levels in 23 out of 35 asthmatic children and did not find any difference in mean serum IgE values among children presenting with normal or elevated IgM (347.1 IU/ml) values.

Kajosaari et al (1981) observed higher total serum IgE levels in atopic disease.

Srivastava et al (1982) found that serum IgE level was elevated above control level in all the three groups (age of onset, periodicity and duration of disease) of patients. However, within a particular group no difference was noted in IgE level on the basis of duration and periodicity of disease. Level of IgE tended to be lower in patient with late onset asthma as compared to early onset asthma, but this difference was not statistically significant.

Herbert et al (1982) in their study of 72 cases found serum IgE value of over 150 KU per litre in 51 atopic asthma cases who showed positive skin test to 5 common allergens.

Tong et al (1986) found elevated total serum IgE levels in all 30 patients of extrinsic asthma. The range in age for all patients was from 4 to 13 years, with a mean of 8.2 years.
Khatua et al (1987) studied 59 random cases of bronchial asthma in children. Total serum IgE level measured by paper radio-immunosorbent test (PRIST) ranged from 25-580 KU/L except in cases with ascariasis who showed a range of 1410 - 2215 KU/L. Total serum IgE was higher in the higher age group of patients and in those who had a family history of allergy, more than 8 attacks in a year, positive radio-allergo-sorbent test and a sensitivity to larger number of allergens. The severity of the disease was not related to total or specific IgE.

THE CLINICAL RELEVANCE OF IgE:

Handerson (1971) showed that determination of serum IgE level did not help in any way, in the diagnosis and management of asthma and rhinitis. Similarly, loeffler (1973) demonstrated its uselessness in the diagnosis owing to wide variation observed in blood levels.

Orged (1975) demonstrated that elevation of serum IgE level at or before one year of age was highly correlated with atopic disease in the first two years of life. The elevation preceded the manifestations of atopy. Author concluded that IgE could be useful in
the prediction of allergy in small children with hereditary predisposition. Kjellman (1976) also demonstrated a rise in serum IgE level, 6 months prior to the onset of allergic symptoms.

Use of serum IgE to differentiate atopic from nonatopic dermatitis, rhinitis and asthma has been questioned as O’ Loughlin (1977) found raised level in many dermatoses and Nagaya (1979) proposed that there was no level of IgE, which could be used to rule out the presence of allergic disease.

Wang and Patterson (1979) established the use of serum IgE measurement in the diagnosis and follow up of patients of bronchopulmonary aspergilosis (Nelson 1982).

Kajosaari and Searlnen (1981) showed that IgE could also help in the prediction of allergic disease among children with bronchiolitis, but single measurement of IgE was not useful.

Nelson (1982) examined the impact of the discovery of IgE on the clinical practice of allergy in 3 major areas.

(i) Use of measurements of total and specific IgE in the diagnosis of allergic disease.
(ii) To study the natural history of the development of allergic disease and study the impact of allergic immunotherapy.

(iii) To define significant allergens and cross allergenecity and to assess the quality of allergy extracts.

Bousquet et al (1984) discussed the predictive capacity of cord blood IgE in the development of allergy, in infancy and childhood. They opined that the risk of developing atopic disease (recurrent wheezy bronchitis and atopic dermatitis) was 5-10 times higher when the initial IgE was above +1SD than when it was below this limit. Authors felt that the best predictive capacity was shown when both the family history of atopy and the titration of cord serum IgE were combined.

Johnw xynginger (1989), while quoting many authors explained that elevated levels of total serum IgE in bronchial asthma could help in the diagnosis. But, the author has cautioned that in other diseases also serum IgE level was raised viz - parasitic infestation, immuno-deficiency, allergic rhinitis etc.
COMPLEMENT SYSTEM IN BRONCHIAL ASTHMA:

The name "complement" was initially chosen to describe the heat labile property of serum to complement the ability of antibodies to lyse red blood cells or bacteria. Today the name "complement" stands for a highly complex, multimolecular, self-assembling biologic system that constitutes one of the major humoral mediators of inflammation.

The absence of deficiency of complement component has been recognized in persons with a wide variety of human diseases as well as in normal individuals. Complement deficiencies may be hereditary or acquired. Complement deficiencies are uncommon. However, some of the deficiencies are associated with characteristic clinical syndromes (Nusinow et al 1985).

Nomenclature of complement:

The term complement is applied to a system of factors, occurring in normal serum, which are activated characteristically by antigen-antibody interaction and subsequently mediate a number of biologically significant consequences. Study of the nature of complement has been concentrated to a large extent on the analysis of process of immune haemolysis and nomenclature proposed for
complement is based primarily on the haemolytic sequence. Complement, as it participates in immune haemolysis, comprises 9 components. It now appears established that these 9 factors are essentially similar, although not necessarily interchangeable, into species most studied (Austen et al 1968).

**THE COMPONENTS OF COMPLEMENT:**

A numerical notation is used for those complement components which participate directly in the reaction of immune haemolysis. Hitherto the numbers have been preceded by the symbol C'. It is now suggested that this usage be changed and that the symbol C be used to denote complement components.

In the order of their reaction the complement components should therefore, be designated C1, C2, ..., C9. The first component of human complement comprises 3 distinct protein sub components to which the provisional names C1q, C1r and C1s have been given. C1q was previously known as the 11s component or C'9 (Austen et al 1968).

The interaction between antigen and antibody can alter the configuration of a particular site in Fe region of the antibody molecule and make a receptor for the operation of first fraction (C1q) of first
component of the complement. Once the first fraction gets a place in the immune complex, following interaction between antigen and antibody, it acquires the ability to activate the rest of the complement components one after another in a sequence C1, 4, 2, 3, 5, 6, 7, 8 and 9 till a puncture or functional hole in the cell membrane is made and lysis of the cell occurs (Das Gupta 1976).

There are two main pathways of complement activation classical and alternate or properdin. In classical pathway the interaction starts at C1 level and finishes at C9 until cell lysis occurs and Fe portion of immunoglobulin is involved. Whereas, in alternate pathway the reaction start at C3 and is independent of Fe region and is usually poorly lytic. Once C3 is activated the remainder of components are activated in a standard cascade. The end point is lysis of the target cell by a complex consisting of C5b, 6, 7, 8, 9. The classic pathway may be activated by antigen antibody complexes and nonimmunologically by C reactive protein and trypsin like enzymes (Behrman and Vaughan 1989).
Halprin et al (1973) observed decreased arteriovenous levels of complement in occupational asthma after bronchial challenge with fungal antigens.

Kay et al (1974) observed in their study that there was no significant difference between the circulating levels of C3 and C3 proactivator when adult and child asthmatics were compared with their respective normal controls. Moreover, the adult asthmatic patients had a higher total haemolytic component level ($C_{50}$) than adult controls. But, differences between child asthmatics and the control subjects were not significant. These workers also found that a raised C4 level was associated with the features of allergic disease whereas, those with non allergic disease had low C4 level.

Codfrey et al (1975) reported that estimation of C4 levels did not prove useful in the classification of asthma since a normal C4 level were found in asthma patients.

Delancy et al (1976) observed normal C3, C4 complement and total haemolytic component levels in sixteen asthmatic patients with aspirin idiosyncrasy.
Arroyave et al (1976) detected the presence of activated C3 and factor B components by counter immunoelectrophoresis in the serum of asthmatic patients, who were challenged with skin test positive antigen, thus proving the activation of alternative pathway of complement system.

Weemass et al (1977) estimated significantly depressed C4 and C3 proactivator levels in child asthmatic patients as compared with controls.

Hutchcroft et al (1978) also found normal complement component levels (C3, C4, CH$_{50}$) in seven allergen induced asthmatic patients with no evidence of complement activation.

Steven et al (1979) observed a significant decrease in CH$_{50}$ and non-significant decrease in C3 levels in eight patients, who showed positive bronchial reaction to allergen challenge.

Baur et al (1980) estimated significantly increased complement component levels (C3 and C4). Moreover, increase in CH$_{50}$ level was seen in five out of sixteen asthmatic patients, during an immediate asthmatic reaction. The levels were also raised in seven patients during late asthmatic reactions.
Srivastava et al (1982) estimated complement component levels (CH<sub>50</sub>, C4 and C3 proactivator) in one hundred thirty patients with bronchial asthma and fifty five healthy subjects. In sixtytwo patients the onset of the disease was before the age of 20 years. In sixty seven patients the asthmatic symptoms were of less than 5 years duration. Positive skin tests and family history of atopy were frequently seen in patients with early onset asthma. They observed a significantly decreased C3 level in patients suffering from perennial asthma and in those cases, who had a longer history of the disease. They did not observe any change in C3 proactivator and CH<sub>50</sub> levels in asthmatic patients. Further, they found a significantly raised C4 level in patients with late onset asthma as compared to those with a history of early onset asthma.

Stevan et al (1985) found increased levels of complement component (C3, C4) in asthmatic patients.

**EOSINOPHIL COUNT IN BRONCHIAL ASTHMA:**

Eosinophil luckocyte are characterised by large coarse granules of prominent red colour seen after staining with Romanwasky stain and having a neucleolus with
single or two segments. They normally accounts for fewer than 5% of circulating leukocytes. Eosinophil count may be depressed by high levels of Adreno Cortical hormone and increased in parasitic and allergic disorders. Eosinophil count more than 5% in peripheral blood smear or 250 cells/mm³ is considered elevated. Blood eosinophil in the allergic disorder does not exceed 15-20% but may occasionally be as high as 35%.

In asthma eosinophilia plays a dual part: protecting the patient from the effects of mast cell vasoactive mediators and simultaneously damaging the bronchial mucosa. Eosinophil neutralizes the slow realising substance (SRS) of anaphylaxis and histamine by enzymatic action and by phagocytosis. In course of neutralization of slow realising substance (SRS) of anaphylaxis eosinophil may undergo degranulation or autolysis, causing the release of major basic proteins. These major basic proteins damage the respiratory mucosa in concentration as low as 10 µg/litre (Wasserman et al 1975).

Bray GW (1931) and Smith (1931) found that eosinophilia is predominantly associated with allergic disorders.
Lowell (1967) reported that measurement of total eosinophil count in circulating blood was helpful in the evaluation of asthmatic disease. In his study 28 patients and elevated eosinophil count (7350/mm$^3$). He also noticed that eosinophilia was lacking in patients of bronchial asthma as a result of intercurrent infections or because of eosinophil suppression by bronchodilator drugs.

Orkankis et al (1970) found eosinophilia in 85% patients of bronchial asthma.

Sharma et al (1974) observed elevated eosinophil count in 71.8% patients of bronchial asthma.

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

Shahi et al (1976) found that in 24 patients of bronchial asthma total eosinophil count was significantly higher (441 ± 384/cmm) than in control cases (119 ± 88/cmm). But no correlation was observed between the eosinophil count and T or B lymphocyte counts.

Agarwal et al (1979) in his study found that patients with bronchial asthma had significantly high absolute eosinophil count 917.71 ± 618.9 compared to control cases (231.4 ± 105.4/cmm). A direct correlation
was observed between absolute eosinophil count and T cells percentage.

Arshod (1981) observed eosinophilia in bronchial asthma.

In 1982, Lukza et al in his study found that acute asthma was associated with eosinopenia while chronic and stable asthma showed eosinophilia. The detail of observations are as follows:

<table>
<thead>
<tr>
<th>Type of asthma</th>
<th>Absolute eosinophil count</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute asthma</td>
<td>$170 \times 10^9$ litre</td>
<td>21 $\times 10^9$ litre</td>
</tr>
<tr>
<td>Chronic</td>
<td>$2340 \times 10^9$ litre</td>
<td>1048 $\times 10^9$ litre</td>
</tr>
<tr>
<td>Stable</td>
<td>$1950 \times 10^9$ litre</td>
<td>345 $\times 10^9$ litre</td>
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Acharya et al (1983) carried out their study in childhood asthma. They studied 300 cases of childhood asthma, diagnosed clinically and found eosinophilia in 45.3% of the cases which were having absolute eosinophil count $7400$ cells/$mm^3$ while 710% eosinophilia was found in 23% cases and 740% eosinophilia was observed in 5 out of 300 cases.
SPIROMETRY IN BRONCHIAL ASTHMA:

Pulmonary function studies are essential for diagnosing and assessing the severity of asthma in patients. Objectives measurements of lung function for monitoring asthma are analogous to measurements in other chronic disease situations, for example measuring blood pressure with a sphygmomanometer for hypertension (Kjellman et al 1992).

Estimation of ventilatory capacity helps in the treatment of bronchial disease. Some diseases cause narrowing of the airway during expiration such as asthma and chronic bronchitis. The forced expiratory volume (FEV), forced vital capacity (FVC) percentage are reduced some times to 40% or less. This is due to a greater reduction in FEV than FVC (Davidson 1986).

FVC (forced vital capacity) is the largest volume of air measured on complete expiration after the deepest inspiration, and that expiration being as forceful and rapid as possible. This volume is significantly reduced in chronic restrictive pulmonary disease due to air trapping (Guyton 1991).
FEV₁ (Forced expiratory volume) is usually calculated in one second. This tests the volume of air exhaled over a given time period, during the performance of a forced expiration. If it is below the predicted normal volume, then this gives information regarding the severity of the expiratory airway restriction.

FEF (forced expiratory flow) formerly called MEF₂₅, MEF₅₀, MEF₇₅ (maximum expiratory flow rate). This is the average rate of flow for a specified portion of the forced expiratory flow, usually calculated between 200 ml and 1200 ml on the chart. A slowed rate is an early sign of chronic obstructive pulmonary disease. Patient is normal if his one second rate is not below 70 percent. If it is below 70 percent, he is likely to have some obstructive disease such as bronchial asthma, chronic bronchitis or pulmonary emphysema. If one second volume observed after the administration of a bronchodilator, shows an improvement of 20% or more the patient probably has bronchial asthma which is distinct from pulmonary emphysema (Guyton 1991).

In case of obstructive disease such as pulmonary emphysema or bronchial asthma, the bronchiolar collapse occur during forced expiration. This is called as "check value" effect.
When treating asthmatic patients, it is often desirable to make frequent objective assessments of PEF, usually more than once a day. Daily or circadian variation in PEF reflects the severity of asthma (Kjellman et al, 1992).

In case of bronchial asthma the FEV/FVC percentage is greatly reduced, sometimes 20% or less in reference to normal control, which is between 68-80% (Guyton 1991).

Pulmonary function testing is valuable in the evaluation of children in whom asthma is suspected. In those known to have asthma, such tests are useful in assessing the degree of airway obstruction (Behrman and Vaughan 1987).