Although cotton and flax have been used into the manufacture of textiles, since times of antiquity, byssinosis does not seem to have been recognised, until the introduction of mechanized process in the early nineteenth century. The departmental committee on compensation for card room workers adopted in 1939 the term "Byssinosis", since then it has appeared extensively in literature dealing with respiratory diseases of the textile workers.

The word 'Byssinosis' is derived from Greek 'Buddos' or Latin 'Byssus' meaning flax. Hirt (1871) classified it as one of the diseases produced by the dust and he preferred to call it "Pneumoconiosis Lyssinotica". It was proved that there was cotton in the lungs; however, this disease could not be called as "Cotton Pneumonia" and to be more representative, it was called "Lyssinotic Pneumoconiosis" or, in short, "Pulmonary Lyssinosis". Hirt possibly, due to clerical error, added the word "Lyssinotica" (from Greek, Lyssarage, fury), but Proust, in 1877, used the correct terminology for the disease "Byssinosis".

It is important to note here that apart from byssinosis, other conditions affecting the respiratory system like mill fever, weaver's cough, matteress maker's fever, chronic bronchitis, etc., are also observed in the workers exposed to cotton, flax and soft hemp dusts in different parts of the world.
Mill fever is the reaction that occurs in some people when they first come into contact with cotton, flax or soft hemp dust. Symptoms include malaise, cough, fever, chills and upper respiratory tract disorders. These symptoms may last for a few days or weeks and then pass off automatically with subsequent continued exposure to dust. It has been referred to by many other names such as "card room fever," "cotton fever," "cotton cold," "dust fever" and "heckling fever" in flax workers. Its prevalence is difficult to assess but variously estimated from 10 to 80% (Harris, 1972; Uragoda, 1977). Whether or not mill fever predisposes to the subsequent development of byssinosis is not known, but according to Gill (1947), byssinosis did not occur in the absence of a preceding history of mill fever. The cause is uncertain, but may be due to endotoxins of contaminating Gram negative bacteria in the vegetable dusty air of the mill (Rylander and Lundholm, 1978a).

Weaver's cough is an acute respiratory illness identical with late asthma, but is accompanied by fever and malaise in those who have been exposed to mould-contaminated yarns that have been treated with flour paste or tamarind seed extract (Murray et al., 1957). Acclimatization does not occur among the workers, so both new and old long established workers are equally affected.

Mattress maker's fever is again an acute respiratory illness. It affects both established cotton workers and new workers exposed to stained cotton. Symptoms appear within the first six hours of exposure, with fatigue and generalized aching, anorexia, headache, nausea and vomiting which follow. Symptoms last for two to five days. The cause
was attributed to contamination of cotton by Gram negative bacillus, \textit{Aerobacter cloacae} and the disease may well have been in a form of extrinsic allergic "alveolitis" (Neal et al, 1942).

There is ample evidence that chronic bronchitis is far more common among byssinotic cotton textile mill workers (Merchant et al, 1972) which is indistinguishable from that found in other chronic bronchitic conditions. This condition may progress to the point of disability. The relationship of bronchitis to byssinosis is a complex problem. Kay (1831) recognised it as a separate condition, but Collis (1908) did not think that there was a clear distinction between the two diseases, to enable the physician to differentiate them.

The symptoms of humidifer fever are found remarkably similar to those of byssinosis (Pickering et al, 1976). In view of the fact that cotton mills are kept at the high humidity, the possibility of contamination of the humidifying plant may be responsible for respiratory illness, at least in some cases in cotton mills.

Cotton is the downy cellulose fibre which covers the seeds of the cotton plant (\textit{Genus Gossypium}, family \textit{Malvaceae}). Cotton plants grow in warm and dry climates. The cotton and the seed inside it make up the cotton boll which is picked up by hand or machine when fully mature. The bract and pericarp at the base of the boll and occasionally a short length of twig are broken off with the boll in hands picking. In mechanical picking more of the plant including the leaves and stem may be picked. The bolls are passed through ginning process to separate the seeds and other materials from the cotton, which is then packed and compressed into bales for the spinning mills. The cotton is mechanically cleaned, drafted, and spun and then wound into finished yarn in successive
stages in spinning mills. 'Trash' is the plant debris and soil from the parent plant. The grade of cotton depends upon colour and 'trash' content which can be addressed visually. 'Trash' content is expressed as a percentage of the total weight of the raw cotton. 'Fly' is the cotton and very large airborne particles seen by the naked eye in the cotton mills. It consists mostly of broken cotton fibres up to an inch length and pieces of plant debris too large to enter the lungs.

Byssinosis is primarily a problem among the subjects working in the opening and carding areas of cotton mills. Three stages are recognised in the development of byssinosis. The first stage of byssinosis is commonly called as 'Monday feeling' or 'Monday Sickness'. The symptoms begin after long exposure to cotton dust and usually occur in workers who have the histories of sufferings from mill fever on the very beginning of joining the work in the cotton industry. Afterwards, workers may remain quite well for more than 10 years even except for a slight cough. Suddenly the cough becomes aggravated and exceedingly irritating or the workers do feel attacks of chest tightness and breathlessness. These symptoms usually occur on Monday or after the break day and the worker feels well for the rest of the week. This condition may persist without getting worse, until the worker leaves the industry. In the second stage, the symptoms extend for more days in a week and finally become permanent. Removal of worker from exposure to cotton dust during the first stage of byssinosis can result in complete cure, but symptoms recur suddenly and with great severity if work at the mill is resumed. If the exposure continues, attacks of bronchitis or asthma follow. Intervals or absence from work becomes necessary. Even at this stage recovery can occur, if exposure to cotton dust is terminated and the
individual can be rehabilitated in some other job. Many workers who reach to the second stage do not leave the industry and pass into the third stage of disabling byssinosis.

In the third stage, the symptoms of chest tightness and dyspnoea are so distressing that the worker has to leave the cotton industry. Though he will have some relief when he is away from cotton dust, dyspnoea remains as a permanent disability. The disease progresses to chronic bronchitis with emphysema, cough with muco-purulent sputum. But there is no fibrosis and, therefore, characteristic X-ray findings are absent. There is a progressive reduction of ventilatory capacity. Intradermal prick tests are usually found negative with cotton extracts.

Much of the work in Britain in the 1950's was pioneered by Schilling, and his system of grading is still currently and widely used, to classify byssinosis in the epidemiological studies (1963). Vegetable dusts known to cause byssinosis are cotton, flax, soft hemp and sisal. Other vegetable dusts which, in high concentrations, may cause irritation of the respiratory tract, without characteristic symptoms of byssinosis, are given in Table-1.

Cotton industry is the largest industry which carries a risk of byssinosis. Cotton mills can be classified according to quality of raw cotton which they spin and the fineness of the yarn which they produce. Coarse mills usually process cotton of low grade and short fibre; whereas fine mills usually process cotton of high grade and long fibre. In most of the cases, byssinosis only develops after a long term exposure like ten years or more to cotton, and five years or more to flax or hemp. Byssinosis occurs throughout the world where cotton, flax and soft hemp fibres are being processed. The prevalence of byssinosis in cotton
<table>
<thead>
<tr>
<th>Main Effect</th>
<th>Plant</th>
<th>Source of Fibre</th>
</tr>
</thead>
<tbody>
<tr>
<td>Byssinosis</td>
<td>Cotton</td>
<td>Fruit</td>
</tr>
<tr>
<td></td>
<td>Flax</td>
<td>Stem</td>
</tr>
<tr>
<td></td>
<td>Soft hemp</td>
<td>Stem</td>
</tr>
<tr>
<td></td>
<td>Sisal</td>
<td>Leaf</td>
</tr>
<tr>
<td>Non-specific Effect</td>
<td>Jute</td>
<td>Stem</td>
</tr>
<tr>
<td>Irritation</td>
<td>Sunn (Indian hemp)</td>
<td>Stem</td>
</tr>
<tr>
<td></td>
<td>Henequen</td>
<td>Leaf</td>
</tr>
<tr>
<td></td>
<td>Mauritius hemp</td>
<td>Leaf</td>
</tr>
<tr>
<td></td>
<td>Manila hemp</td>
<td>Leaf</td>
</tr>
<tr>
<td></td>
<td>St. Helens hemp</td>
<td>Leaf</td>
</tr>
</tbody>
</table>

*Schilling, 1981.*
workers varies according to the quality and quantity of 'responsible' dust in the working environment.

The first comprehensive study on general prevalence of byssinosis in cotton industry was reported by Schilling in Lancashire Cotton Mills (1956). He found prevalence of byssinosis, 40% among card room workers of coarse cotton mills. Roach and Schilling (1960) reported prevalence of byssinosis, 51% among card room workers, and 41% among blow-room workers of coarse cotton mill; while only 6% among card room workers of fine mills. El Batawi (1962) studied prevalence among cotton ginnery workers in Egypt where the prevalence of byssinosis was 27% among card room workers; while 38% among ginners. A study from Netherlands showed 14% prevalence rate among card room workers of medium cotton mills (Lammers et al, 1964). Belin et al (1965) showed 62% prevalence rate of 'Monday dyspnoea' among card room workers of fine cotton mills in Sweden. They did not attempt a grading system as described by Schilling, and used the term 'Monday dyspnoea' to define byssinotic subjects.

Similarly, the word 'Monday feeling' was used by Dingwall-Fordyce and O'Sullivan (1966) in a survey of 22 waste cotton mills. The unusual grading scheme adopted in this study was probably due to the fact that the experimental work was carried out in 1950, before Schilling had introduced his widely accepted grading system. Prevalence of 'Monday feeling' was 30% among card room workers, and 62% among workers of raw cotton industry. Studies from the U.S.A. have shown similar prevalence rate of byssinosis among card room operatives as found elsewhere, i.e. 26% among coarse cotton card room workers (Bouhuys et al, 1969a), 25% among medium cotton card room workers (Zuskin et al, 1969), 20% among modern cotton and synthetic blend card room workers (Merchant et al, 1972),
37% and 40% among medium and coarse cotton mill card room workers, respectively (Molyneux and Tombleson, 1970).

In a study of cotton ginneries in Sudan, Khogali (1969) had to adopt a different method of diagnosis as the workers operate a 7 days week. Byssinosis was defined as chest tightness on return from annual holidays and continuing for at least three consecutive days during the first week of ginning. Prevalence of chest tightness was 20% among cotton ginneries workers. A study from Tanzania showed 22% prevalence of byssinosis among card room workers and 26% among blow room workers (Mustafa et al, 1979).

There are few reports on prevalence rate from India also. Gupta (1958) surveyed textile mills of Ahmedabad and examined 253 workers of card and blow rooms who had worked for minimum of six years continuously, and also 251 workers (as control subjects) in other departments, viz., weaving, sizing, dyeing, bleaching, cloth and miscellaneous departments. There was no incidence of byssinosis in control subjects as compared to 6.3% incidence in cardroom workers. Siddhu et al (1966) reported the prevalence rate of byssinosis 3.47% among card room workers of cotton mill of Kanpur. Kamat et al (1981) from Bombay reported the initial prevalence of byssinosis 14% in card room workers. They also reported that the prevalence of both byssinosis and bronchitis increased with a longer service. Maldhure et al (1982) reported the prevalence of byssinosis 17.6% among card room workers of cotton mill of Nagpur. They also found a positive association of prevalence with length of service.

It was thought that byssinosis only occurs, to an appreciable extent, in blow and card room workers. Schilling (1956) found a prevalence of byssinosis 7% among spinners of a coarse cotton mill and Roach
and Schilling (1960) found only 2% among spinners of coarse cotton mill. High prevalence rate was found in U.S.A. from coarse cotton mill, but this higher values of prevalence was attributed to the presence of winding machine in spinning room (Bouhuys et al, 1969a). However, 5 to 12% prevalence rate of byssinosis have been reported by many investigators from spinning rooms of both coarse and medium cotton mills (Zuskin et al, 1969; Molyneux and Tombleson, 1970; Schrag and Gullett, 1970; Fox et al, 1973; Mustafa et al, 1979). Mekky et al (1967) showed that 19% of winders and beamers had byssinosis. Recent increase in prevalence rate of byssinosis in processes subsequent to blow and card rooms could be the contribution of greater awareness about the disease. Nevertheless, despite many differences in methodology and even in the exact definition of byssinosis used, byssinosis prevalence figures have been found to vary between 10% and 60% or more for blow room and card room workers. Prevalence figures have been found generally lower in spinning and winding areas. Coarse cotton mill workers have shown greater prevalence of byssinosis than medium cotton mill workers and fine cotton mill workers showed lowest prevalence rate.

A number of investigators have recorded dust concentration in working areas of the mills where the incidence of byssinosis had also been determined. In early studies, only total dust was measured (Roach and Schilling, 1960; El Samra et al, 1972). Later on, many investigators used hexhlet with horizontal elutriator for the collection of dust samples and the dust was separated into three fractions coarse, medium and fine (Wood and Roach, 1964; Molyneux and Tombleson, 1970; Mekky et al, 1967; Berry et al, 1973). The reason behind dividing cotton dust into fractions depending on their size was based on investigations of
deposition of particles within the bronchial tree. Deposition of the particles depend on gravity, inertia and sedimentation. Greater the inertia, more is the possibility of deposition in the upper airways, especially in the nasopharynx. Sedimentation is influenced by the density and square of the diameter of the particles. Smaller and lighter particles penetrate faster down into the lungs. Diffusion or Brownian motion occurs if the particles are smaller than about 0.5 μm and is important only in the terminal respiratory unit. It has been worked out diagramatically (Task Group of Lung Dynamic, 1966) which illustrates nasal, tracheobronchial and pulmonary deposition as function of particle size for a respiratory rate of 15 minutes and tidal volume of 750 cc. Nearly all particles > 10 μm are deposited in the nasal passages but most particles of 1 μm diameter reach the pulmonary areas (i.e. terminal and respiratory units). Fibres behave as a chain of fine particles and their deposition is determined by their diameter rather than their length.

Dust levels measured in cotton manufacturing areas can be influenced by number of factors like the type of sampler used for the measurement, the duration of the sampling period, the location of the sampler relative to the dust producing operations, the type and grade of cotton being processed, the type of operations being carried out on the cotton, the speed at which equipment is operated, air-conditioning, location of air inlets and the dust controls. According to Barr et al, (1974) it is hard to arrive at a general figure for dustiness which might be representative of the cotton industry as a whole.

Few reports are there, where no correlation has been found between dust concentration and prevalence of byssinosis. Belin et al
(1965) studied workers in four Swedish cotton mill (card rooms) and they reported the lowest byssinosis prevalence in the mill with lowest dust concentration (31% byssinosis, total dust 2.19 mg/m$^3$, fine dust 1.65 mg/m$^3$). No correlation was reported in other three mills between dust concentration and byssinosis. Braun et al (1973a) also observed no correlation between total or fine dust fractions and the prevalence of byssinosis. Hence they concluded that the increased prevalence of byssinosis among card room workers must be due to the composition of card room dust rather than the amount present. Merchant et al (1972) measured dust concentration using cyclone separator in a modern mill blending cotton and synthetic fibres. Low concentration of fine dust ($\leq 2$ mm) was found in carding (0.2 to 0.3 mg/m$^3$) compared to spinning department (0.62 mg/m$^3$). Total dust was also higher in spinning (1.84 mg/m$^3$) compared to carding (0.58 mg/m$^3$). However, byssinosis prevalence was found to be 20% in the preparation areas; whereas it was only 2% in the processing areas. Therefore, it was concluded that total dust gave no indication to byssinosis. As the sample size for fine dust was too small, no conclusion was given for possible correlation with byssinosis. Lammers and co-workers (1964), in a comparative study on English and Dutch mills, reported higher total dust concentration in the card room of English mill (2.9 vs. 1.9 mg/m$^3$), but the fine dust concentrations remained same. However, prevalence of byssinosis was 13.5% and 17% for English and Dutch mills, respectively. Concentrations of both total and fine dust were less in spinning rooms of English mill (0.4 vs. 2.6 mg/m$^3$), but byssinosis prevalence was similar to that of spinning room of Dutch mill (1.5 vs. 1.6%).

However, majority of investigators have reported a correlation
between dust concentration measured by static samplers and byssinosis prevalence.

The first extensive study was carried out by Roach and Schilling (1960) to investigate the correlation between dust levels and prevalence of byssinosis. For the dust collection, hekhlet was used in three coarse and two fine cotton mills and total dust concentration was also measured. Among workers exposed to an average total dust concentration of more than 2.5 mg/m³, there was a high prevalence rate of byssinosis. But workers exposed to dust concentration of less than 1 mg/m³ did not develop byssinosis. They had decided the following classification for workroom exposure limits as measured by static samplers.

Table-2
CLASSIFICATION FOR WORKROOM EXPOSURE LIMITS

<table>
<thead>
<tr>
<th>Grade of Dustiness</th>
<th>Concentration of Total Dust (mg/m³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Safe, with medical supervision of workers</td>
</tr>
<tr>
<td>2</td>
<td>Dust control desirable and medical supervision essential</td>
</tr>
<tr>
<td>3</td>
<td>Dust control and medical supervision essential</td>
</tr>
</tbody>
</table>

* Roach, and Schilling (1960).*
By combining the results of total 8 studies, a direct relationship has been established between total dust concentration and byssinosis prevalence, as shown in Table-3.

Table-3  
BYSSINOSIS PREVALENCE AND RELATIONSHIP BETWEEN TOTAL DUST CONCENTRATION

<table>
<thead>
<tr>
<th>Total Dust (mg/m³)</th>
<th>Prevalence of Byssinosis (all grades in %)</th>
<th>No. of Workers Examined</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0 - 0.5</td>
<td>1.5</td>
<td>212</td>
</tr>
<tr>
<td>0.5 - 1.0</td>
<td>2.8</td>
<td>108</td>
</tr>
<tr>
<td>1.0 - 2.0</td>
<td>9.9</td>
<td>1259</td>
</tr>
<tr>
<td>2.0 - 3.0</td>
<td>8.5</td>
<td>1226</td>
</tr>
<tr>
<td>3.0 - 4.0</td>
<td>34.0</td>
<td>465</td>
</tr>
<tr>
<td>4.0 - 5.0</td>
<td>55.0</td>
<td>245</td>
</tr>
<tr>
<td>5.0 +</td>
<td>27.5</td>
<td>92</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>3607</strong></td>
<td></td>
</tr>
</tbody>
</table>


Measurement of total dust has its own advantages. However, it is unlikely to provide an adequate index of byssinosis risk, because of relative amount of fly and the finer dust fractions are subject to variability both within the mill and also from one mill to another. For this reason, the current hygiene standards are based on dust measurement excluding fly.
The Occupational Safety and Health Administration has established a permissible exposure limit of 200 $\mu$g/m$^3$ for yarn manufacturing; 750 $\mu$g/m$^3$ for slashing and weaving; and 500 $\mu$g/m$^3$ for all other processes in the cotton industry and for non-textile industries, where there is exposure to cotton dust. The standard specifies that concentration is to be measured with a vertical elutriator cotton dust sampler or its equivalent (Federal Register, 1978).

There are certain reports indicating the dust particle size and its impact on the prevalence of byssinosis. According to Molyneux and Berry (1968), prevalence of byssinosis among card room workers correlated best with the concentration of medium dust particles, while Cinkotai (1976), by analysis of his earlier data, came to the conclusion that the best correlation of byssinosis prevalence could be obtained with the 1-2 $\mu$m and 2-4 $\mu$m particle size fractions of the cotton dust. A statistically significant association between prevalence of byssinosis and the concentration of fine dust was reported from Sudan (Khogali, 1969). In a later follow-up study, Khogali (1976) measured the medium dust concentration (less fly) and, again, showed a significant correlation between dust concentration and prevalence of byssinosis.

In determining the risk of developing byssinosis, the duration of exposure of a person in the cotton mill is an important factor. Effects of total exposure time to cotton dust on prevalence of byssinosis have been studied by a number of investigators. Fox et al (1973) and Khogali (1976) reported that the degree of correlation between static sampled dust levels and frequency of byssinotic symptoms was increased by including a time factor. By expressing the dust exposure
as mg. year/m³, Fox and his co-workers (1973) were able to predict that about 10% of subjects exposed to 0.5 mg/m³ of dust for forty years would develop symptoms of byssinosis. They also observed that the frequency of byssinotic symptoms increased rapidly with the exposure time up to twenty years and thereafter decreases. This might be due to the less resistant workers who develop disabling byssinosis leave employment prematurely. This ‘survivor population’ effect has been noted by many investigators.

There are some studies demonstrating a high prevalence of byssinosis even in workers with only a short exposure to cotton dust.

Zuskin and Valic (1972) studied two groups of female workers. The prevalence of byssinosis was lower in the group of 69 workers who had a mean duration of exposure of 16 years (17.4%); whereas 60 workers with a mean duration of exposure of 4 years had prevalence rate 28.5%. Thus, prevalence of byssinosis was lower in the workers with long duration of exposure than in those with a shorter duration. Bouhuys et al. (1969a) studied 214 male workers of whom 45% had been exposed for 1 year or less in carding and spinning areas and very few exposed for more than 10 years. They reported 20% had symptoms of chest tightness. However, in this study, 80% of the workers were heavy smokers. Haglind et al. (1981) showed a prevalence of byssinosis (19%) in 248 workers of 5 Swedish cotton mills and reported that prevalence was not related to duration of employment when age was a controlled variable.

It is known that cigarette smoke causes a decrease in clearance rate of inhaled particles from lungs and the delayed process might lead to inhaled textile dusts to remain in contact with the bronchial tree.
for more time, thus causing a greater pathophysiological effect in smokers. In many epidemiological surveys, effects of smoking on prevalence of byssinosis and the decline of lung function during a period of years at the mill have been studied. The increased prevalence of byssinosis was found among workers having smoking habit in comparison to non-smokers, considering age, sex and duration of employment at the mill (Schilling, 1964; Bouhuys et al, 1969a). Bouhuys et al (1969a) showed that this increase in prevalence rate occurs in all grades. Elwood (1965) reported similar finding among flax workers.

Many investigators from other countries have also shown that smokers have a greater risk of developing byssinosis (Fox et al, 1973; Berry et al, 1974; Clonfero et al, 1976; Noweir et al, 1975a); however, there are contradictory reports too (Gandevia and Milne, 1965; Braun et al, 1973c; Khogali, 1976; Haglind et al, 1981). Thus the prevalence of byssinosis appears to be related with number of interacting factors i.e., age, duration of exposure, type of exposure, personal habits like smoking etc.

Other vegetable dusts, like flax, soft hemp and sisal, are concerned, very less number of people are exposed to these dusts due to occupation. Hence, very few reports on the prevalence of byssinosis among the workers in these industries are available.

Flax is one of the groups of bast or stem fibres which forms the fibrous bundles in the inner bark of stem of dicotyledon plants, mainly grown in temperate regions. Flax fibres are obtained from the stem and are extracted by retting or soaking in water followed by...
hand or mechanised separation of the fibres from the outer covering.
Fibres are used for making linen cloth, towelling, flax twines, nets
and ropes.

Mair et al (1960) showed that flax workers in Dundee suffered
a reduction in ventilatory capacity on Monday morning suggesting the
disease was similar to that of cotton workers. By using the standard
questionnaire coupled with lung function tests, Bouhuys et al (1961)
demonstrated the presence of byssinosis among flax workers. They
reported that there were no complaints relating to the symptoms of
byssinosis among workers handling retted flax in the open air, sug­
gestin that the disease was caused by inhalation of airborne dust
which was likely to be present in much more quantity during indoor
work. They reported 67% (ungraded) prevalence of byssinosis among the
workers exposed to dust during indoor work. Elwood (1965) investigated
the effect of the type of processing in the flax mill on the prevalence
of byssinosis. Prevalence among preparers (including hecklers and
carders) was 54%; among other preparers (including drawers, doublers,
comblers, rovers and dry spinners) was 27%; among wet finishers
(including wet spinning and polishing) was 0.4%; among other workers
such as maintenance was 42%. According to Noweir et al (1975a), in
Egyptian flax industries, the prevalence of byssinosis among batting
workers was 30% where the total dust concentration was 17.4 mg/m³ and
respirable dust concentration was 2.98 mg/m³. Prevalence among hack­
ling and combing workers was 37% where total dust concentration was
61.0 mg/m³ and respirable dust concentration was 9.15 mg/m³; while in
spinning, the prevalence was 21% with a total dust concentration of
8.5 mg/m³ and respirable dust concentration of 1.54 mg/m³.
Zuskin and Valic (1973) reported higher prevalence of byssinosis in a group of seasonal workers who were exposed only for two or three months in a year. Noweir et al (1975b) also reported a 37% prevalence of byssinosis in seasonal flax workers, which was higher than that found in the employees working throughout the year. It was found that the trend of byssinosis in the flax industry was similar to those found in the cotton industry; and employees of flax industry developed byssinosis after a relatively short exposure to flax dust. Bouhuys et al (1963) suggested that the treatment of the flax was important in the etiology of byssinosis. Employees working with chemically pretreated flax did not get the disease, suggesting that this treatment removes or destroys, or someway modifies the agent(s) responsible for byssinosis; whereas biological retting of flax did not.

Hemp is a bast (or stem) fibre from the plant Cannabis sativa grown throughout Europe and Asia. Hemp, like flax, was among the first fibre used by man from a very early date. There are two distinct types of hems, the hard fibres which are derived from the leaf of the plant, and soft fibres obtained from the stem. The majority of investigations about byssinosis among hemp workers have concentrated on the soft hemp processing industry. Valic et al (1968) showed prevalence of byssinosis (40.6%) in Yugoslavian soft hemp industry. In a comparative study of hemp, flax, cotton, jute and sisal workers, Valic and Zuskin (1972) reported prevalence of byssinosis for workers in hemp (44%), flax (43%), cotton (27%) and jute and sisal (0.1%). In this study they included only female non-smokers belonged to the age group of 22-29 years with exposure of 2-7 years, and the mean dust concentration remained in the
range of 1.92 to 4.24 mg/m³. So, this restricted the size of population studied and thus the results were not statistically valid as might have been desired. A series of studies on soft hemp workers in Spain were carried out by Bouhuys et al (1967; 1969b) and Bouhuys and Zuskih (1976). They examined the workers of two factories which processed bacterially-retted soft hemp. The results showed that 77% of the workers had byssinosis of Grade I and II working in the plant with only natural ventilation as compared to 33% in the plant with exhaust ventilation in the dusty areas. Here also the number of workers was small.

Very little work has been reported on the concentration of hemp dust and its possible relationship to byssinosis. Bouhuys et al (1967) collected dust using an electrostatic sampler and did not find a direct correlation between dust concentration and changes in FEV₁ during Monday, so they could not correlate the dust concentration to the prevalence of byssinotic symptoms. They also reported that there was no association between the prevalence of byssinosis and length of exposure to dust. Valic et al (1968) also measured the dust concentration using an electrostatic precipitator but they did not attempt to correlate it with prevalence of byssinosis.

Sisal, a native of Mexico and Central America, is mainly cultivated in Hawaii, East and West Indies and East Africa. Sisal fibres are separated from the leaves by wet retting or deccortification. After drying under the sun, the fibres are taken to the brushing department where the fibres are softened, cleaned, combed, and finally used for baling. Very little work has been reported about prevalence of byssinosis in sisal factories. Earlier work indicated that there was no problem
of byssinosis in the sisal industry (Gilson et al., 1962; Valic and Zuskin, 1972). However, recent studies of Mustafa et al. (1970) on Tanzanian sisal workers has shown classical symptoms of byssinosis. In this study, 77 sisal spinning workers and 83 brushing workers were included. The prevalence of byssinosis was found to be low in spinning department (5.2%), but was very high in brushing department (48.2%) where the workers were exposed for longer period (11.8 ± 7.3 years), as compared to spinning workers (2.9 ± 2.6 years). Stott (1958) showed that the dust concentration was six times higher in brushing than spinning department in a Kenyan sisal factory.

Cotton and other vegetable dusts have been classified into coarse, medium and respirable dusts. Cotton dust contains in varying proportions all parts of the cotton plant. The potential for cotton trash to produce fine particulate material is determined by the friability of its components. Bract, the leaf-like structure, which enfolds the cotton boll and wood fragments are the most friable and, thus, the most abundant 'respirable' (less than 10 μm) components of raw cotton (Morey, 1979).

Studies in cotton textile mills have shown that the incidence of byssinosis can be correlated with the average concentration of fine cotton dust (Merchant et al., 1973; Fox et al., 1973; NIOSH, 1974) and with duration of occupational exposure (Fox et al., 1973; NIOSH, 1974). Imbus and Suh (1973) reviewed the complex chemical composition of cotton mill dust found in various processing operations. The range of chemical contents was enormous. It contained organic and inorganic materials. Dust composition was found to vary in the proportions of all plant parts, i.e., leaf, bract, capsule and lint, as well as
of fibres fungi, bacteria, inorganic materials and materials from other contaminating vegetation (NIOSH, 1974). Dried plants material was classified by Wakelyn et al (1976) into carbohydrates (cellulose, hemicellulose and pectins), lignins, tannins (condensed and hydrolysable phenolic compounds (terpenoids, coumarins, flavanoids), porphyrins, lipids, proteins, glycoproteins and many miscellaneous compounds like mono and disaccharides, amino acids, amines, aminopolysaccharides, essential oils, histamine and 5-hydroxytryptamine.

Causative agent in byssinosis has been shown to be a water extractable, filterable, non-volatile agent (40°C) which can be retained on dialysis (Hamilton et al, 1973). Cellulose, a major constituent (about 95%) of the raw cotton fibre has no reported implication in byssinosis. Lignins are polymers of phenylpropane units and are not water soluble, so are unlikely to be involved in byssinosis. Lacinilene C-7 methyl ether, a terpenoid, has been reported by Lynn et al (1974) to be a major chemotactic agent and histamine releaser in bract and cotton dust. Of the coumarins, scopoletin was found to release histamine via direct activation and among the flavonoids catechin and quercetin also found to release histamine via direct activation (Ainsworth and Pilla, 1982). According to Kilburn et al (1973) quercetin also caused leucocyte recruitment through airway walls.

Roach and Schilling (1960) analysed nitrogen content of cotton dust by Kjeldahl's method and used this as index of the amount of proteins present. They reported fine dust (< 7 μm) which contained 21-27% protein, medium dust (7 μm to 2 mm) which contained 14-21% protein, and coarse (> 2 mm) which contained 3.8% protein. Massoud and
Taylor (1964) and Ainsworth (1975) have suggested an immunological pathogenesis to byssinosis. Evans and Nicholls (1974) have suggested that the main histamine releasing component of cotton dust was a polysaccharide-protein complex. Mohammed et al (1971) isolated free sugars from cotton dust (glucose, mannose, galactose and fructose), and reported that D-glucose in the aqueous extract could cause contraction of guinea-pig ileum. They also isolated amino polysaccharide (byssinosan). Nicholls and Skidmore (1975) showed that byssinosan was capable of contracting guinea-pig ileum and thus demonstrated its pharmacological activity.

Hedin et al (1975) isolated 158 different compounds, mainly essential oils, in a steam distillate of cotton waste. However, none of these compounds were water soluble. Cotton dust was also found to contain histamine and 5-hydroxytryptamine (Maitland et al, 1932; Battigelli et al, 1977). Earlier work of Antweiler (1961) and Bouhuys et al (1960) suggested that histamine content was too small to produce direct respiratory effects comparable to those found in byssinosis. Inorganic content of cotton dust was also found quite high 43% (Fornes et al, 1976). Various minerals were found in the dust, although in most cases no relation was established between mineral content and byssinosis. However, according to Charles and Manzel (1975) NH₄⁺ and SO₄⁻² ions could cause histamine release in the lung tissue. Brown et al (1980) suggested that the silica content of dust might play a role in the etiology of byssinosis. Another source of minerals in the atmosphere of textile mills is the humidification plant. Batra et al (1980) and Roberts et al (1980) have shown that the humidification plant contributes significantly to the concentration of dust in workroom atmosphere and, therefore, presumably to its inorganic content.
Organic fibres, such as cotton and flax, carry several kinds of micro-organisms on their surfaces. These micro-organisms are normally found on all plants and the condition of this symbiosis is reflected by difference in the number of organisms found on various kind of plants (Young, 1977). Microbial genera identified in the airborne dust samples or plant parts are common air, water or soil borne microbes and would be expected to be associated with plant materials. Among Gram negative, *Acinetobacter*, *Agrobacterium*, *Alcaligenes*, *Enterobacter*, *Escherichia*, *Flavobacterium*, *Klebsiella*, *Pseudomonas*; among Gram positive *Bacillus* and *Clostridium*; and among fungi *Alternaria*, *Aspergillus*, *Cladosporium*, *Fusarium*, *Nemodendrum*, *Mucor*, *Penicillium* and *Rhizopus* genera were found (Tuffnell, 1960; Rylander et al, 1975; Welty et al, 1977; Cinkotai et al, 1977; Rylander and Lundholm, 1978a; Fischer, 1979; Simpson and Marsh, 1982).

Not only the micro-organisms were associated with dust, but their metabolic products were also found. Two important products of microbial origin are thought to be associated with byssinosis are bacterial endotoxins and proteases.

In recent years Gram negative bacterial endotoxins and its relation in the causation of byssinosis have been studied in-depth. Endotoxin is the lipopolysaccharide that comprises a major portion of the cell wall of the Gram negative bacteria. The endotoxins from each species of bacteria are different, but lipid A moiety is similar for Enterobacteriaceae and has similar series of biological actions regardless of its source. Endotoxins from Gram negative bacteria can cause a multitude of biological effects and initiate a chain of secondary reactions involving inflammatory, haemodynamic and immunological responses (Bradley, 1979; Morrison and Ryan, 1979).

An association between bacteria on cotton plants and pulmonary illness was first suggested by Neal et al (1942). They examined the samples of cotton used and exposed animals and humans to the dust or extracts thereof. They concluded that the illness was caused by the inhalation of Gram negative bacteria or their products which were present on stained cotton and its dust.

In 1961, Pernis et al showed that histamine or histamine-like substances were liberated by endotoxins and by saline extracts of card-room waste cotton by guinea-pig ileum method. They emphasized that the cotton extracts were pyrogenic in rabbits and could induce "tolerance". Rabbits tolerant to cotton extract were tolerant to endotoxin and vice-versa. Cotton extracts also caused leukopenia followed by leukocytosis. Material isolated from ordinary raw cotton was pyrogenic and Schwartzman active and human experiments after inhalation of endotoxins caused fever, malaise, and decreased vital capacity.
Cinkotai et al. (1977) and Cinkotai and Whitaker (1978) studied the extent of subjective byssinotic symptoms around the Lancashire in cotton spinning and cotton waste mills, willowing mills, a wool spinning and tea-packing plant and pipe tobacco factory. Measurements were made of dust concentrations (total dust less fly), airborne microbes and LPS in the various work places. Employees at the plants were investigated for symptoms of chest tightness, using standard questionnaire. They did not find any correlation between the dust concentrations and byssinotic workers; in fact, only few byssinotic workers were found in some of the very dusty mills, while other cleaner mills showed a high prevalence rate. The correlation between symptoms, prevalence and the amount of airborne Gram negative bacteria was highly significant. A relation between byssinosis and airborne LPS was found. This was statistically significant if all the plants investigated were included in the analysis; but just below the border line of significance if only the cotton mills were analyzed.

A study on the cotton mill workers in Sweden indicated that the prevalence of byssinosis was related to the number of airborne viable Gram negative bacteria as well as to the dust level in different mills (Haglind et al., 1981).

Rylander (1981) studied the average FEV₁ over the Monday shift among the employees of 23 U.S. cotton mill workers, and correlated it with the vertical elutriator dust level and the number of Gram negative bacteria present on the bale cotton processing. Decrement in FEV₁ was poorly correlated with the dust concentration. However, a significant correlation was observed when the exposure was expressed as number of Gram negative bacteria in an equation weighting dust levels in plants.
and the number of employees. The dose response relationship suggested a threshold value of about $10^3$ Gram negative bacteria per gram of bale cotton.

The concentration of endotoxin found in dust appears to vary enormously. Pernis et al (1961) were the first to demonstrate the presence of LPS in cotton dust which was about 3 to 10 mg/g of cotton dust. Cinkotai et al (1977) reported the first epidemiological study using the Limulus lysate method for the determination of LPS concentration in cotton mills. In card room air, the concentration of LPS was in the range of 0.2 to 1.6 μg/m$^3$. Similar results were reported by Fischer (1979). Values ranging from 0.3 to 2.5 μg/m$^3$ were reported by Bergstrom et al (1980) in an experimental card room where ordinary bale cotton was carded under the condition resembling to those in cotton mills.

Byssinosis prevalence was found to correlate very well with the level of endotoxin concentration in the dust. Cavagna et al (1969) measured the amount of endotoxins in the dust as well as in the air of cotton and hemp mills. They observed 32% prevalence of byssinosis in cotton card room workers and 47% in hemp card room workers. The airborne concentrations of endotoxin in cotton and hemp card rooms were 7.2 μg/m$^3$ and 8.7 μg/m$^3$, respectively. They found no case of byssinosis either in the cotton spinning room or hemp roving room where the airborne concentrations of endotoxin were 0.8 μg/m$^3$ and 0.36 μg/m$^3$, respectively. They explained this zero prevalence by suggesting that the active agent, whether endotoxin or some other materials, could be below the required concentration to cause sensitization.
Fischer (1980) studied the correlation between Gram negative bacterial count, airborne endotoxin concentration and dust concentration with the change in FEV₁. They observed much lower count of Gram-negative bacteria in the air of spinning areas as compared to those observed in the air of carding areas of the mills. All the above mentioned parameters were correlated well when all the departments of mill were included.

Inhaled particles are deposited at various levels of respiratory tree according to their size. A maximum penetration down to the deeper parts of the lung takes place for particles smaller than around 2 μm. Most airborne bacteria, if occurring in single cell and a considerable proportion of industrial dust, fall into this category.

Gram negative bacteria and endotoxins are present in a variety of different environments. However, information about the particle size distribution is scanty. In cotton cardroom 97% of the particles have been shown to be smaller than 3 μm, and 70% to be smaller than 0.5 - 0.7 μm (Haglind et al., 1981). Aerosol of Gram negative bacteria have a particle size of 1-3 μm, whereas aerosolized endotoxins in water solution is a molecular aggregate of LPS. Substances deposited in the deeper parts of lung may be transferred to the pulmonary capillaries and distributed by the blood. This exposure route, hence, bypasses the hepatic circulation where the liver acts as a major detoxifying organ for endotoxins (Utili et al., 1977).

The reactions of endotoxins after inhalation are less studied. Effects of endotoxins after inhalation are found different from those caused by intramuscular or intraperitoneal administration. This might
be due to differences in the concentration at the cellular level or due to differences in the type of cellular reactions initiated at the site of administration (Rylander and Snella, 1983).

Many investigators have reported the effects of inhaled endotoxins on the lungs with the particular reference to the development of clinical diseases. Maier et al. (1981) injected \( ^{125} \) labelled *Escherichia coli* 0111: B4 LPS intravenously into rabbits. Around half the dose was found in the tissue macrophages of the liver. Tissue samples from liver, spleen, lung, kidney, adrenal, heart, skeletal muscle, lymph node and small intestine showed an accumulation of LPS in tissue macrophages; whereas hepatocytes and endothelial cell did not contain any LPS. Within the tissue macrophages, LPS was localized in phagosomes. In the spleen some LPS was found in neutrophils. In the lungs an intravascular accumulation of neutrophils and monocytes was observed and some of these cells contained LPS. In the liver tissue macrophages, there was no sign of LPS degradation after 3 hours. The pulmonary accumulation of neutrophils caused by LPS cleared more rapidly in LPS resistant mice (Walker and Fletcher, 1981).

The chief cell in the alveolar region responsible for defence against external agents is the macrophage. Maier et al. (1981) and Rosenstreich and Vogel (1980) suggested that this cell was the primary target for endotoxins after inhalation. The alveolar macrophages have a multitude roles, including uptake of particles, regulation of immune response and secretion of various substances which control the activity of other cells. It has now been recognized that the main role of macrophage is to act as the leader of cellular orchestra, thus tunes other cell types which are responsible for the final pathological effects.
Endotoxins in the contact with macrophages were taken up by pinocytosis into lysosomal vesicles within 10 to 15 minutes (Bona, 1973). Inside the macrophages, endotoxins affect a variety of functions such as attachment to surfaces, phagocytosis via C3 receptors and the secretion of hydrolytic and other enzymes. Other affected systems are the secretion of endogenous pyrogens, tissue factors, plasminogen activators, substances influencing T and B lymphocytes, neutrophils and platelets. The latter cell types can, in turn, affect the function of macrophages, both by inhibiting and by further stimulating their initial activity. It has been shown that LPS-induced macrophage activation may be mediated by lymphocytes (Ryan and Yohe, 1981). The macrophage is also a major source of prostaglandins, PGF2α, which acts as a potent bronchoconstrictor (Elissalde et al, 1980).

Macrophages are known to inactivate endotoxin, but the extent to which this represents a major defence mechanism under condition when endotoxin is inhaled, is not known. Maier et al (1981) showed in vitro that 1 μg LPS/ml in a culture of tissue macrophages, produced a 5 to 6 fold increase in lactate dehydrogenase, lysozyme and plasminogen activators production over a 4 days incubation period. Different results were observed after inhalation of endotoxins. In guinea-pigs acutely exposed to an aerosol of *E. coli*, LPS decreased the enzyme secretion from pulmonary macrophages. This decrease was observed 4 hours after exposure and was maximum at about 24 hours, and thereafter the values returned to normal (Heland et al, 1982).

A classic effect caused by LPS was neutropenia occurred rapidly after the exposure (Ulevitch and Johnston, 1978). Experimentally it has been demonstrated after bolus injection of 0.5 μg of *E. coli* or *Salmonella*
The neutropenia was caused by migration and extravasation of neutrophils and was followed by leukocytosis, reflecting a mobilization of neutrophils and/or neutrophil precursors from the bone marrow (Mechanic et al., 1962).

Wilson et al. (1981) suggested that LPS did not act directly upon neutrophils and did not stimulate metabolism or enzyme release. They proposed that these effects were due to a LPS effect on serum with possible activation of complement and a subsequent effect on the neutrophils.

In animals and humans exposed to Gram negative bacteria by inhalation, the initial reaction was an increase in the number of neutrophils in the airways, beginning a few hours after exposure and reaching a maximum after about 24 hours (Rylander and Snella, 1976; Rylander and Lundholm, 1978a). At a considerably higher dose levels (50 µg/kg), however, Goodman et al. (1979) reported extravasation of neutrophils into the alveoli. Similar findings were reported by Guenter et al. (1981) after the application of higher doses.

Bomski et al. (1971) showed that workers in cotton mills, where the dust contained a large number of Gram negative bacteria and endotoxin, had an increased number of neutrophils in their blood with a tendency in some groups to lower values on the last working day in the week. The neutrophil increase in the airways was dose dependent (Helander et al., 1982) and caused by the lipid A part of the LPS molecule (Helander, 1982). The reaction was species specific, with hamsters the reaction was rather unsensitive, while in guineapigs and man it was more sensitive. Studies using animals, where more than 95% of the serum complement had been inactivated by cobra venom showed that
inhaled LPS still caused a neutrophil accumulation in the airways (Snella and Rylander, 1982).

Migration of neutrophils, however, occurred against supernatants from cultures of Gram negative bacteria and the supernatants contained the endotoxins (Helander and Lounatmaa, 1981). An alternative mechanism for the increase of neutrophils in the airways after exposure to endotoxin or endotoxin containing dusts such as cotton dust may be a direct action of endotoxins on neutrophils without the involvement of macrophages.

Endotoxins increase stickiness of leucocytes and decrease chemotaxis (Ginsburg and Quie, 1980). Preliminary data from experiments on students exposed to cotton dust, which always contained endotoxin, have shown increased stickiness of neutrophils and decreased in vitro migration capacity at the end of dust exposure (Rylander, 1981). Yamada et al (1981) demonstrated that endotoxin activated neutrophils adhered to and damaged endothelial cells in vitro and that this effect was caused by release of superoxide anions and $\mathrm{H}_2\mathrm{O}_2$. This mechanism could explain the invasion of blood cell elements into the alveoli and the increased penetration of plasma into the lung after inhalation of endotoxin (Fischer et al, 1977).

The presence of an increased number of neutrophils in the lung tissue could cause an increase in the burden of free oxygen radical released by neutrophils (Staton et al, 1981). Free oxygen radical may react with the tissue and cause the release of arachidonic acid, vasoactive prostaglandins, thromboxane or prostacyclins, leading to the development of acute pulmonary inflammation (Rylander and Snella, 1983).
A major pulmonary response after an inhalation exposure to Gram-negative bacteria or purified LPS was augmented in the number of macrophages and neutrophils in the airways (Rylander and Nordström, 1974; Rylander and Snälla, 1976; Walker et al, 1975; Hudson et al, 1977). An augmentation of the number of neutrophils on the nasal epithelium has been demonstrated in workers in cotton mill card rooms (Merchant et al, 1975) and among workers in an experimental card room, as well (Bergstrom et al, 1980).

LPS injected intravenously had a very high affinity for platelets (Evans, 1972) by which it was transported to the liver. At higher doses, platelets were aggregated and subsequent inflammation and damage to endothelial cells occurred (Urbaschak et al, 1979). The platelet aggregates also released vasoconstrictor and possibly bronchoconstrictor agents (Blaisdell et al, 1970).

Using release of (\textsuperscript{3}H)-serotonin from platelets as a measure of platelet secretory response, Morrison et al (1981) demonstrated Salmonella minnesota LPS caused a dose-dependent release, reaching a maximum after about 60 minutes. Complement was probably of importance for platelet aggregation.

After repeated LPS exposures, platelet aggregation in rabbits occurred faster and was partly reversible (Bult and Herman, 1979). The modification of the response was probably due to the presence of antibodies to the polysaccharide part of LPS (Walker and Beasley, 1980). Platelet aggregation could also be induced by serotonin secretion from macrophages (Blumenthal et al, 1980) and by complement split products like C3a, C5a, the latter being about 50 times more active (Meuer et al,
Rabbit platelets aggregated when exposed to 25 μg LPS/ml, however, no aggregation of human platelet could be demonstrated (Abdelnoor et al., 1980).

Whether the changes in platelet aggregation demonstrated in animals are of any relevance for the reactions occurring after inhaled endotoxin in man is not known. According to some reports, after inhalation peritoneal macrophages from rats and mice could secrete a factor which aggregates platelets and could cause release of serotonin from them (Mencia-Huerta and Benveniste, 1979; Blumenthal et al., 1980). Whether pulmonary macrophages secrete platelet activating factors under normal conditions or after in vivo exposure to endotoxin is not known.

In humans, Bomski et al. (1971) showed that the number of circulating platelets in card room workers decreased over the first working day of the week. The decrease in platelets was probably dependent upon intravascular complement activation (Ulevitch and Cochrane, 1978).

Hawinger et al. (1975) demonstrated that Salmonella enteritidis LPS at a concentration of 200 μg/ml could cause release of serotonin from human platelets ranging from 37 to 81%. No platelet destruction, as measured by lactate dehydrogenase release, was found. They also demonstrated an unmasking of platelet phospholipid (platelet factor 3) and this was found to be specific for endotoxin.

The histamine release is a classic reaction in byssinosis research and has been extensively elaborated upon in both animal and human experiments (Bouhuys et al., 1960). As shown by several researchers, LPS can induce the release of histamine (Pernis et al., 1961; Hinshaw et al., 1961; Davis, 1963). The mechanism by which LPS causes histamine
release is not clear. Potential mechanisms are an influence of macrophages on platelets, disruption of neutrophils with release of intracellular histamine or effect on mast cells.

A typical reaction after exposure to cotton dust or extract thereof is a decrease in the pulmonary airflow. Few studies have been performed on this reaction after LPS exposure. Cavagna et al (1969) exposed normal subjects and subjects with chronic bronchitis to an aerosol containing 40 to 80 µg of purified Escherichia coli LPS in 2 ml of saline solutions. In two of eight normal subjects a significant reduction in the FEV₁ was seen after inhalation of 80 µg of LPS. The reaction was present in large proportions of the subjects with bronchitis, in whom it was more pronounced and occurred at lower doses. Exposures to considerably lower doses of LPS were performed by Muittari et al (1980) in a study of bath water disease. Using tap water containing 1 µg of LPS/ml, a 1 ml inhalation challenge brought about a decreased lung diffusion capacity.

Fever and respiratory disturbances are the most important clinical manifestations produced by endotoxins. It is well known that exposure to endotoxin, LPS and lipid A causes fever in animals and man but with development of tolerance after repeated exposures.

LPS is well known pyrogen. Rylander (1981) observed several cases of mill fever among laboratory assistants and students at the stage of beginning of the work in an experimental card room. The development of tolerance to the fever inducing effect of LPS is well known from animal experiments (Wolff, 1973).
According to Elin et al (1981) the dose required to produce fever in human after intravenous administration is 0.1 to 0.5 ng/kg. Guinea pigs exposed to an aerosol of soluble lipid A from Enterobacter agglomerans at an estimated lung dose of 0.1 μg/kg developed fever with a maximum period of 3 hours (Helander, 1982). Among workers exposed to dust containing endotoxins, fever develops in cotton mill workers (mill fever), mattress makers (mattress fever), and in office staff working in premises which are ventilated with air contaminated from humidifiers (humidifier fever).

Several hypotheses have been suggested concerning the mechanism for fever. Neutrophils are known to release endogenous pyrogen (EP) and endotoxin is one of the substances which can induce the release of EP (Collins and Wood, 1959). They also demonstrated that neutrophils from tolerant donors released the same amount of EP as normal cells. Murphy et al (1981) suggested that EP was identical with lymphocytes activating factors produced by rabbit alveolar macrophages and this information could again point out the importance of pulmonary macrophages for the fever reactions occurring after inhalation of endotoxins.

According to Rylander and Snella (1983), persons exposed to airborne dust containing endotoxins developed a bronchoconstriction during the exposure. The constriction was found different from the asthmatic airway response. It developed progressively over several hours, reaching maximum at about 6 hours. This increase in bronchoconstriction was used as a diagnostic criterion for byssinosis - a syndrome developing among workers in the cotton and flax industries (Schilling et al, 1955).

Whether or not this reaction develops after exposure to endotoxin in pure form at a similar dose level is still being debated. Pernis et al,
(1961) exposed 3 persons to 15 to 60 μg *Escherichia coli* LPS by inhalation. A reduction in FEV₁ was found shortly afterwards. In the second exposure, 4 days later, with two of the same subjects, 60 μg LPS caused the same symptoms and slight fever. Cavagna et al. (1969) exposed human subjects to an aerosol of *Salmonella typhi*, LPS 40–80 μg for 15 minutes. Out of the 8 subjects, 2 showed a decrease in FEV₁. Out of 7 persons with chronic bronchitis, two reacted with a decrease of FEV₁ which was higher as compared to controls.

These data shows that bronchoconstriction could be induced after exposure to large doses of LPS. It cannot be ruled out, however, that in working situation in card rooms the particles or some chemicals in the dust could also play a role in the development of bronchoconstriction. If the observed decrease in FEV₁ in cotton card room workers was due to endotoxin, a possible mechanism could be the above mentioned mobilization of neutrophils into the airways and the subsequent release of tissue-irritating substances, either directly from neutrophils or via platelets. Secretion of prostaglandin from macrophages might be of another possibility.

Prolonged exposure to airborne irritant, such as air pollutants and cigarette smoke, may bring about a development of mucus hypersecretion, goblet cell hyperplasia and chronic cough. This condition – chronic bronchitis – has been diagnosed among non-smokers exposed to endotoxin containing dust such as cotton and flax dust. Snell (1966) exposed rabbits to an aerosol of LPS for several months. Histological preparations demonstrated the development of goblet cell hyperplasia and increased mucus secretion. Similar results were also reported by
Pernis et al (1961). Among humans, Pratt (1981) showed that globlet and bronchial cell hyperplasia were found among non-smokers in cotton mills. The changes were more pronounced among smokers. Cavagna et al (1969) exposed rabbits to Escherichia coli LPS for 20 weeks. Histological examination after the exposure demonstrated the development of bronchitis. Chronic bronchitis has been found among smoker as well as non-smoker cotton mill workers.

Presence of airborne proteases in causation of byssinosis can not be ruled out although little work has been carried out especially on the aspects of pathogenesis. There are reports showing the correlation between airborne proteases concentration and prevalence of byssinosis. Tuma et al (1973) found significant correlation between airborne proteases concentration and symptoms of byssinosis in 14 out of 17 mills. Using probit analysis they found a significant correlation between acid protease, neutral protease or chymotrypsin-like enzymes as the independent variable and with a drop in FEV\textsubscript{1} or chest tightness as dependent variable. The level of significance was further increased after omitting three mills which operated a screening programme for recruiting the employees and had full medical monitoring programme. Chinn et al (1976) examined proteases levels and the prevalence of byssinosis in willowing mills. Proteases concentration was 0.64 µg/mg in mill dust and 10.7 µg/m\textsuperscript{3} in mill air (the American Conference of Governmental Industrial Hygienists, 1971 recommended a TLV of 0.3 µg/m\textsuperscript{3}). However, they found the prevalence very low. Cinkotai and Whitaker (1978) reported a significant correlation between proteases concentration in the air and prevalence of byssinosis in 21 cotton mills. de-Treville (1971) compared byssinosis prevalence with atmospheric
proteases concentration. A significant correlation between the number of workers who experienced a decline in FEV\textsubscript{1} of greater than 10% over a work shift and proteases concentration. However, no correlation between the number of workers with chest tightness on some or all Mondays and proteases concentration was observed. Similar byssinosis like symptoms were observed among detergent manufacture workers exposed to proteolytic enzymes derived from the selected strain of *B. subtilis* (Greenberg et al, 1970; Webster et al, 1972). Among various bacteria found in cotton dust are members of genus *Bacillus* (Welty et al, 1977). According to Braun et al (1973b), fungi including *Aspergillus* could be the source of these airborne proteases. As very little work on animal experiments and clinical studies have been carried out, it is difficult to assign the specific role of proteases in the aetiology of byssinosis. However, its role cannot be ruled out.