

Organic dusts – from knowledge to prevention

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RYLANDER R. Organic dusts — from knowledge to prevention. *Scand J Work Environ Health* 1994;20 special issue:116—22. Vegetable, animal, and microbial aerosols (organic dusts) induce a variety of pulmonary disease and subjective symptoms. This review presents the pathology and clinical symptoms related to organic dust exposure. Most of the symptoms are related to inflammation, which is not unexpected in view of the many inflammatory agents present in organic dusts. Prevention is primarily a matter of dust control, information, and medical surveillance. In the future, specific agents like bacterial endotoxins should be controlled.

KEY TERMS — (1→3)-beta-D-glucan, chronic bronchitis, endotoxin, hypersensitivity, inflammation, pulmonary diseases, review, toxic pneumonitis.

Vegetable, animal, and microbial matter are ubiquitous in the environment of humans and under normal conditions present no risk to health. When organic dusts are aerosolized and inhaled, however, they can attain concentrations that overwhelm the normal defense mechanisms of the body and result in disease.

Humans have probably been aware of disease brought about by organic dust ever since farming practices were introduced, some 6000 years ago, although the first known recorded accounts of symptoms came much later. In 1555, the Danish bishop Olaus Magnus (1) described a disease among threshers: "When separating the grain from the chaff, care must be taken to choose a time when there is a suitable wind which will sweep away the grain dust, so that it will not damage the vital organs of the threshers. This dust is so fine that it will almost unnoticeably penetrate into the mouth and accumulate in the throat. If this is not quickly dealt with by drinking fresh ale, the thresher may never again or only for a short period eat what he has threshed."

About 150 years later, the Italian physician Ramazzini, in his book *De Morbis Artificum Diatriba* (2), described the same special symptoms among farmers. The typical symptoms after the inhalation of molds, an important component of many organic dusts, were described by Floyer in 1726 in his book *A Treatise of Asthma* (3).

With the industrialization of fiber treatment, particularly cotton, pulmonary disease was described among children working in Lanchashire cotton mills and among spinners in these mills (4, 5).

In view of the large number of persons exposed in the cotton industry, disease caused by cotton dust became a focus of interest. Proust was the first to use the term "byssinosis," derived from the Egyptian word for "small fiber" (6). In 1936, Prausnitz (7) described the typical symptoms as follows: "After working for years without any appreciable trouble except a little cough, cotton mill workers notice either a sudden aggravation of their cough, which becomes dry and exceedingly irritating . . . These attacks usually occur on Mondays . . . but gradually the symptoms begin to spread over the ensuing days of the week; in time the difference disappears and they suffer continuously."

Apart from disabling symptoms from the lung, the exposure to cotton dust also caused increased mortality from respiratory and cardiovascular disease (8, 9).

As new environments with organic dust exposure were found, the diseases observed were named after the particular environment in which they were detected, and a confusing list of names appeared — farmer's lung, mushroom grower's lung, cheese turner's lung, mill fever, humidifier fever, bird fanciers' disease, and the like. The etiology and pathogenesis of these diseases were unknown, and, among them, byssinosis was always considered mysterious, mainly attributable to a particular part of the cotton plant, the bract leaves.

During the last few decades, knowledge of diseases caused by organic dusts has expanded rapidly. With modern epidemiologic methods, reliable incidence and prevalence figures have been obtained, and toxicologic techniques have provided a better understanding of the underlying cell reactions. A comprehensive textbook on organic dusts and their effects has recently been published (10).

This paper gives an overview of the various environments in which organic dust exposure is particularly important, describes the major cell reactions that

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take place after exposure, and suggests a classification for the different clinical entities that occur. Finally, suggestions for the future, with particular reference to prevention, are given. In view of the long tradition of work on cotton dust, many of the examples are taken from that area. The experience from these studies is, however, applicable to other situations of organic dust exposure as well.

Organic dust environments

An overview of different environments with organic dust exposure is given in table 1. The table illustrates the multitude of environments in which organic dust exposure can take place. It is also clear from the table that the exposures are generally mixed — a microbial component is almost always present.

Although it is not always appreciated, the indoor environment is an important source of organic dusts. House dust contains animal proteins and fecal material, material from plants, bacteria, and molds in varying quantities. Molds and house dust mites are particularly important in humid conditions, and airborne molds can attain levels equal to those found in industry or when moldy hay is handled.

To cause an effect, the different organic dusts must be aerosolized. This process can be achieved by machinery, ventilation air, or movement of humans or animals. The particle range is large, but there is always an important fraction of smaller particles. Penetration into the deep parts of the lung is not necessary for effects to occur — deposition in the nose or the larger airways is sufficient.

Cell reactions

The immense development in the understanding of inflammation during recent years (11) has had important implications for the understanding of the pathogenesis of disease induced by organic dust. It is beyond the scope of this paper to describe the complicated events initiating an inflammatory response, but a simplified diagram with respect to organic dusts is presented in figure 1.

The hallmark of the inflammatory response in the airways is the invasion of neutrophils from the lung interstitium and the blood that takes place after acute exposure. After repeated exposure, this response becomes less marked, and instead lymphocytes and eosinophils migrate into the airway epithelium and the airways. In this respect, the inflammation induced by organic dust is similar to the inflammatory response in asthma (12).

Another important cell is the T lymphocyte with its different subgroups. Activation of T cells and a shift in the proportion of different subgroups is a distinctive characteristic of the granulomatous pneumonitis that can develop after organic dust exposure (13). T-cell subgroups are also important for the de-

layed type of hyperreactivity and the acute bronchoconstriction induced by organic dusts (Beijer et al, unpublished manuscript).

Communication between the inflammatory cells occurs by means of mediators such as interleukins, membrane-derived mediators such as prostaglandins, leukotrienes and platelet activating factor, interferon-gamma, and many others (11). Specific mediators for different cell types have been identified and shown to exert both stimulatory and depressing functions. There is no specific mediator for a particular type of reaction — mediators work in conjunction with one another in a mesh-type fashion.

The most important consequences of the application of inflammatory mechanisms to disease induced by organic dust is the relative downgrading of the importance of antibodies. The concept that a type III reaction occurred in the lung, particularly after exposure to molds, is no longer valid (14).

Table 1. Examples of environments with organic dusts.

Environment	Type of activity or area
Agriculture	Handling of grain, crop, hay Greenhouses
Animals	Swine or dairy confinement buildings Poultry or turkey houses and processing Laboratory animals
Waste products	Sewage water and silt Household garbage Compost
Industry	Vegetable fibers (cotton, flax, hemp, jute, sisal, kapok) Sugar-cane processing Fermentation Timber and wood processing Biotechnology processing
Indoor environment	Contaminated water in humidifiers Mold growth on building structures, in ventilation ducts, or other such places

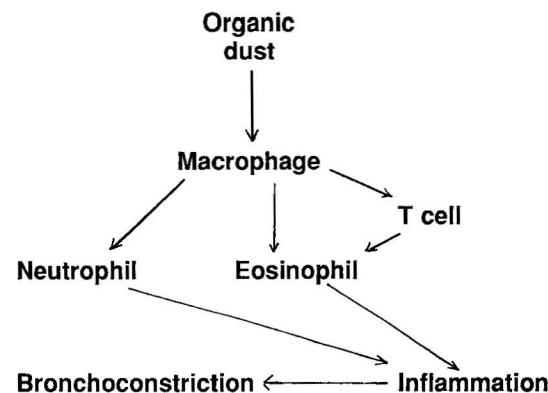


Figure 1. Overview of cellular reactions induced by organic dust exposure.

Effects of exposure to organic dust

It is clear from the preceding sections that organic dusts contain a multitude of specific agents with a potency to initiate many different cellular reactions in the lung and the rest of the body. Protective reactions can also be distinguished, in which the effects mirror the body's normal defense mechanisms and destructive reactions in which the defense mechanisms overreact or are overwhelmed owing either to dose or to exhaustion of the system.

The different lung diseases caused by organic dust exposure are found in table 2. Systemic effects have also been described (10), but are not dealt with in this presentation.

Inflammatory responses

Acute inflammation. The inflammatory response is produced by agents which activate different cells, chiefly macrophages, to excrete inflammatory mediators. The resulting pathology is a toxic pneumonitis characterized by a leaking of plasma from the capillaries into the alveolar and pulmonary tissue, as well as invasion of cells, particularly neutrophils, through chemotaxis. As a consequence, the blood-air diffusion capacity can be decreased (15).

At more severe stages, subjective symptoms in the form of fever, malaise, and other influenza-like symptoms appear. There is a small decrease in air-flow, but no changes detectable by pulmonary X rays. The symptoms usually disappear after 24–48 h, and no sequelae are found. In the literature, this clinical syndrome has often been named after the environment in which it was observed (mill fever, grain fever, humidifier fever, etc), but the terms organic dust toxic syndrome and inhalation fever are also used (16). Toxic pneumonitis can be present without clinical symptoms.

Inflammation can also cause irritation of the eyes, nose, and throat, sometimes followed by a dry cough. As the effects are found in the airways, a decreased airflow develops, together with increased

airway reactivity. This syndrome has recently been called mucous membrane irritation — an operational definition based on information from questionnaires (17).

Chronic inflammation. With increasing exposure time, the acute effects gradually change. The toxic pneumonitis diminishes, although a certain cell infiltration, now in terms of monocytes and eosinophils, remains. In the airways, the continued exposure brings about a change in the epithelial cell structure with an increase in monocytes and eosinophils and an increase in the cell mass of smooth muscles. Clinically this change results in an irritative cough without sputum, a stage which represents a chronic form of mucous membrane irritation.

A particular type of chronic inflammation in the airways is characterized by excess mucus production and is operationally defined as chronic bronchitis. The underlying mechanism is an increase in mucous and subepithelial glands with alterations in the characteristics of the mucus.

The transition from chronic mucous membrane irritation to chronic bronchitis may depend on the duration of exposure, but specific agents or conditions may also be required.

Chest tightness. A subjective feeling of chest tightness on the first days of work was initially described among cotton workers (18). The reaction has been diagnosed from questionnaires evaluating the presence of chest tightness in relation to the first days at work after a break, for example, a weekend. It is now known that this reaction occurs also after exposure to other organic dusts (19).

One of the early observations on chest tightness was that the symptoms became progressively worse over the years and that new workers seldom had typical Monday-related chest tightness. This finding suggests that sensitization takes place to one or several agents in organic dust. No studies have been able to demonstrate the presence of specific antibodies related to the severity of the chest tightness symptoms after cotton dust exposure, and it is more likely that the sensitization is related to changes in cell reactivity.

The underlying mechanism is unlikely to be bronchoconstriction, as chest tightness can also be present when spirometry is normal. It has been suggested that it may be the result of a temporary accumulation of platelets in the pulmonary capillaries after organic dust exposure (20).

Granulomatous pneumonitis. Certain organic dusts can cause a special form of chronic inflammation — a granulomatous pneumonitis (allergic alveolitis, hypersensitivity pneumonitis). The underlying mech-

Table 2. Pulmonary diseases induced by organic dust.

Origin	Disease
Inflammatory origin	Toxic pneumonitis (TP)
	Organic disease toxic syndrome (ODTS), inhalation fever
	Mucous membrane irritation (MMI)
	Bronchitis
	Without sputum (dry cough)
	Excess sputum (chronic bronchitis)
Immunological origin	Granulomatous pneumonitis (allergic alveolitis, hypersensitivity pneumonitis)
	Fibrosis
	Rhinitis
	Asthma

anism is related to altered T-cell function (21). It is characterized by lymphocytosis in the airways, reduced airway flow, and typical X-ray changes caused by the granulomas. The disease can progress to fibrosis. The underlying mechanism is not known, but may be a combination of chronic exposure to molds, altered function of lymphocytes, and a temporary overload of the cellular defense system when high numbers of spores are inhaled.

Immune reactions

An acute reaction which is equivalent to clinical asthma can occur after exposure to organic dusts over several months. It is characterized by a rapid decrease in lung function. The reaction leads to wheezing and breathlessness. It is provoked by cellular reactions including T cells, platelets, and immunoglobulin E antibodies (22). The features are those of allergic asthma, with a latent interval of symptom-free exposure lasting for weeks or months or sometimes several years. Symptoms are usually at their worst early during the workshift. They improve over week-ends and during holidays. Symptoms usually become more severe over a period of weeks or months until the patient is forced to leave work.

Real life

In real-life situations, for instance, when a group of workers exposed to organic dusts are examined, the results from an examination of the individual worker are seldom as clear-cut as has been described. One will encounter a mixture of syndromes — some persons have organic dust toxic syndrome occasionally and mucous membrane irritation most of the time, some persons develop chronic bronchitis, and a few may have developed granulomatous pneumonitis. Different exposure levels to an agent can cause different symptoms which occur on the same occasion or at different times, depending on exposure and host conditions.

Causative agents

Although early concepts implied that the dust particle in itself could initiate a reaction through macrophage activation, it is now understood that the effects of organic dust exposure are caused by biologically active, specific agents in the dust. These may either be part of the dust particle itself such as plicatic acid from cedar wood, or a contamination thereon, such as Gram-negative bacteria on cotton dust.

The knowledge of specific agents is as yet limited, and it is possible that several active agents are still unknown. Table 3 lists some of the most important agents in organic dusts that have so far been shown to be related to different effects.

Bacterial endotoxins seem to be universally present in many types of organic dusts. Since the first reports suspecting a relation between toxic pneumo-

nitic and endotoxin in the early 1940s (23, 24) and endotoxin and byssinosis in the 1960s (25, 26), analytical techniques have been developed making possible the establishment of dose-response relationships. Relations between the over shift decrease in forced expiratory volume in 1 s (FEV_{1.0}) and endotoxin levels in cotton and other organic dusts have been reported (27, 28). An example of such a relationship between endotoxin levels in cotton dust and airway reactivity (29) is shown in figure 2.

Molds and their cell-wall component, (1→3)-beta-D-glucan, are present in many organic dusts. Experience from inhalation experiments demonstrates that (1→3)-beta-D-glucan interferes with the normal inflammatory reaction, that it depresses the formation of antibodies (Rylander and Holt, unpublished manuscript), and that it acts synergistically with endotoxin or other inflammatory agents (30, 31). (1→3)-beta-D-glucan is probably an important agent for the development of granulomatous pneumonitis after exposure to moldy materials such as hay (32).

Several agents cause asthmatic reactions, for example, plicatic acid from Western red cedar, urinary proteins from animals, and enzymes such as proteases from bacteria. These are but a few examples of the different agents that are present in organic dusts and may cause effects when inhaled. An evaluation of these and other agents in organic dusts was recently published (33).

Prevention

Exposure control

In view of the complexity of the exposure and the different agents and diseases involved, the prevention of disease induced by organic dust may appear to be an unsurmountable task. The pragmatic solution is, however, very simple — decrease the dust levels by general or local ventilation. Table 4 demonstrates the utility of such an approach, as undertaken by a group of cotton industries in the United States (34). The technical action undertaken was an overall reduction of dust levels, and the table demonstrates the resulting decrease in the prevalence of

Table 3. Agents in organic dusts and their effects.

Agent	Effect
Plant origin	
Plicatic acid	Sensitization
Plant tannins	Inflammation
Animal origin	
Protein	Sensitization
Microbiological origin	
Bacterial endotoxin	Inflammation
(1 → 3)-beta-D-glucan	Inflammation
Proteases	Sensitization
Mycotoxins	Toxic, mutagenic, carcinogenic

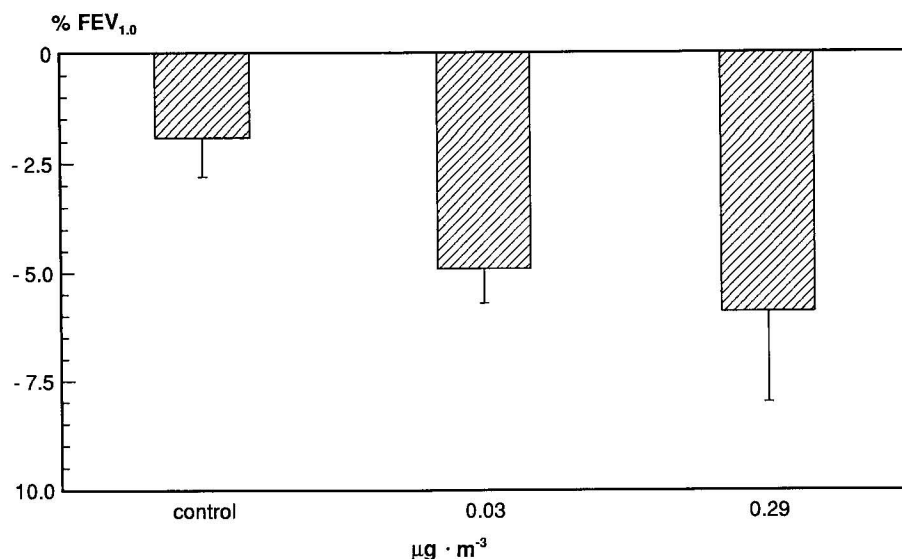


Figure 2. Relation between decrease in forced expiratory volume in 1 s (FEV_{1.0}) induced by 1.25 mg of methacholine and endotoxin levels in cotton dust. Mean decrease (in percent) and the standard error of the mean.

Table 4. Effect of ventilation control on effects induced by cotton dust — percentage of 2000 workers with symptoms. (FEV_{1.0} = forced expiratory volume in 1 s)

Symptoms	Before (%)	After (%)
Chest tightness	4.5	0.6
FEV _{1.0} , overshift decrease > 10%	18	3.5

Table 5. Suggested guidelines for endotoxin limits. (FEV_{1.0} = forced expiratory volume in 1 s)

	Endotoxin limit ($\mu\text{g} \cdot \text{m}^{-3}$)
Toxic pneumonitis	1–2
Chest tightness among workers	0.3
FEV _{1.0} , overshift decrease	0.2
Airway inflammation with increased airway reactivity	0.02

chest tightness and the decreases in FEV_{1.0} induced over a shift among the work force.

There is also, however, a need to control the specific agents present in the dust. Again an example from the cotton industry can illustrate this point. At several mills, technical actions to decrease dust levels have been successful, and the guidelines for cotton dust in the United States, 0.2 mg · m⁻³, were met. After a particularly rainy cotton growing season with increased growth of Gram-negative bacteria on the cotton plant (35), the proportion of endotoxin per gram of dust increased and symptoms were reported, even though the dust level was below the standard. A similar experience was recorded in 1863, when the import of particularly contaminated cotton to Eng-

land caused a large increase in the extent of symptoms among exposed workers in Lancashire (36).

Furthermore, if a mill uses cotton with a very low value of endotoxin, the guidelines may be exceeded without medical consequences. An example is Australian cotton mills, where the endotoxin contamination of the locally grown cotton is very low (37).

These cases illustrate the need for a guideline for specific substances as well, once they are identified and measurement techniques are available. Among the different specific agents in organic dusts, endotoxin is the only one for which guidelines have been suggested, as illustrated in table 5 (20).

Information

Information is a very important part of a prevention program. If workers are informed of the danger and the conditions under which a risk is present, the exposure can be avoided with good work practices. An example is the information program carried out by the Swedish Farmers' Health and Safety Organization, which informed farmers of the risk for granulomatous pneumonitis (allergic alveolitis). Leaflets, lectures, and personal consultations informed of the dangers and how to avoid them. Granulomatous pneumonitis has now practically disappeared in the farming population in Sweden, probably to a large degree as a consequence of this information campaign.

Challenges for the future

There is a great need for information on disease induced by organic dust. Information to the work force

has been dealt with in the preceding section, but there is also a need to inform health personnel and physicians of the problem. Too many physicians still believe that hypersensitivity or allergic reactions are the only relevant effects, and, when the traditional test for allergy, for example, a skin prick test, gives negative results, the patient may be marked as a complainer or as suffering only from subjective (and hence exaggerated) symptoms.

There is also a need for improved diagnostic tools. As regards questionnaires, the British Medical Research Council questionnaire, including additional questions for byssinosis, was the standard for a long time. This questionnaire is no longer sufficient to evaluate all the effects caused by organic dusts. Other forms in which the presence of local and systemic inflammation is evaluated should be used (38).

Spirometry has long been the traditional tool to evaluate effects on the lung. However, this tool is no longer adequate, and new measures, such as tests of airway reactivity, need to be applied on a routine basis.

In the future, additional diagnostic tools, such as measurements of inflammatory mediators and cell function, must be developed. As regards the latter, there are promising results suggesting that changes in T-cell subsets in blood (Beijer et al, unpublished manuscript) or blood monocyte reactivity (39) may be useful for establishing a diagnosis.

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