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Organic dust exposure induced pulmonary damage among livestock workers

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Abstract**—** *Livestock dust contains immunologically potent substances including allergens, endotoxins, microbial compounds, bacteria, fungi, viruses, pathogenic infectious organisms, particulate matter (PM), various poisonous gases such as ammonia, hydrogen sulphide (H_2S), methyl acetate, propanoic acid, heptane etc.It stimulates the immune system through inflammatory and allergenic microbial agents (molds, bacteria, virus and allergens) and microbial-associated molecular patterns (e.g., endotoxin, glucans and peptidoglycans), to result in inflammatory reactions. Farmers are at the risk of developing airway diseases resulting from repeatedly exposures on the livestock farms. There is a paucity of data on in vivo and in vitro cellular and molecular changes following multiple exposures to these livestock contaminants and their long-term impact on the environment as well as human health. The mechanisms of lung dysfunction are still largely unknown. So, there is strong need to look at the combined effect of all the components of livestock dust as stimulatory factors for respiratory hazards. The development of preventive strategies to reduce exposure will be required- in-depth and identification of factors that affect day-to-day variability in exposure.*

Keywords**— Organic dust, livestock dust, endotoxins, respiratory disorders, pulmonary health.**

INTRODUCTION

Livestock keeping is an age-old practice in India andit is the second income generating activity after crop in the agricultural economy of India. Livestock production and agriculture are intrinsically linked to each other and both are crucial for overall food security. About 20.5 million people depend upon livestock for their livelihood. This sector provides employment to about 8.8 % of the population in India and contributes 4.11% GDP of the total Agriculture GDP (25.6%). Unfortunately, livestock farmers are at the risk of developing various diseases associated with exposures to livestock dust.Livestock farming is one of the agricultural industries where farmers are at increased risk for respiratory health problems (Merchant et al. 1991).

Organic dust availability and its composition

In the field of occupational hygiene, airborne and settled particulate material of biologic origin is often referred as organic dust. Organic dusts contain particles of plant, animal and microbial origin (Douwes et al., 2003).Dust exists with heterogeneous composition and this is predominantly organic from animal confinement (Donham, 1986).Organic dusts found in agricultural environments display equally complex composition, although the primary sources may differ. Rylander(1994)reported in animal confinement buildings

some organic dust particles which originated from the animal feed, but the main sources of microorganisms, allergens, and toxins are animal dander, urine, and feces. Microorganisms are widespread in the environment and are often a major component of organic dusts because of the nutrients that the dusts contain. The microflora of organic dust depends on the source material, which depends in turn on a variety of factors, among them substrate composition, acidity, aeration, water availability, and temperature etc. (Lacey, 1994). The main agent in organic dust is endotoxin, a major component of the outer membrane of Gram-negative bacteria, but components of Gram-positive bacteria (peptidoglycans) and fungi (glucans) are also present. The organic fraction of these dusts may contain yeasts, molds, mesophilic and thermophilic bacteria (G-positive and G-negative), histamine, cow urine antigen, mite antigen, endotoxins and pharmaceutical compounds (Donham, 1986; Kullman et al. 1998; Kemper, 2008). Similarly, an "immunoallergic" and inflammatory reaction following the inhalation of organic dust contained in hay among dairy workers due to endotoxins has been proposed to explain this phenomenon (Dalphin et al., 1993; Eduard et al., 2009; Poole and Romberger, 2012). A large number of studies suggested that total dust is comprised of variety of factors such as particle size, concentration of bacterial products LPS and PGN etc. and revealed relevant assessment techniques for the measurement of mold spores, mycotoxins, bacteria, allergenic proteins, endotoxins, and microorganisms in the organic dust (Kirychuk*et al.* 2010 and Hawley *et al.* 2015).

Noxious Gases also act as potential health hazards along with these dust particles such as ammonia which is present inside unbedded dairy calf and hydrogen sulphide which is very poisonous is produced inside the farms during manure agitation (Eduard et al. 2017). Heedreik*et al.* 2007 and Guidry *et al.* 2018 also demonstrated that in animal production farms,the dusts from the animals, their feed, and their faeces contains high levels of poisonous gases such as ammonia (NH3) which comes primarily from the animal's urine and faeces, and hydrogen sulphide (H2S) from manure pits, especially during agitation and emptying. This fact is well supported by Eduard *et al.* 2017 and May *et al.* 2012 that livestock buildings may contain concentrations of contaminants that can negatively affect human health.

As mentioned,in table no. 1.The dust in livestock barns is comprised of molds, actinomycetes, dried fecal matter, pollens , insect parts etc. which means the dust is biologically active and will react to the defense system of the respiratory organs.

Table 1. Classification of dust inside the livestock barns:

Source of dust	**Type of dust**	**Cause of dust**
Grain	Molds, actinomycetes	Storage problem
Hay	Molds, actinomycetes	Poor conservation
Straw	Molds, actinomycetes	Combining/poor conservation
Silage	Molds	Poor conservation
Animal Debris	Faeces,urine,hair,skin,feathers Fungi,bacteria	Animal activity, barn, cleaniless, ventilation,etc.
Feeds	Numerous particles	Feed-distribution/poor ventilation

Source: Air Quality Inside Livestock Barns (gov.on.ca)

Epidemiological Studies

Respiratory disease is an important clinical problem for livestock farmers which significantly increased risk of their respiratory morbidity and mortality. Farmers and other individuals involved in livestock farming have an increased risk for acute and chronic respiratory disorders; their respiration is routinely challenged by intense exposure to several chemical and biological substances such as odorous gases, and organic and inorganic dusts (Schenker *et al.* 1998; Kirkhorn*et al.* 2000; Omland; 2002; Sigsgaard*et al.* 2010). The dairy farmers are exposed to high concentrations of organic dusts, this increased risk seems mainly driven by chronic exposure to these dusts (Basinas et al., 2014; Pfister et al., 2018).

Various studies involving large numbers of exposure measurements which have been published previously for dairy and swine confinement industries have shown that organic dust exposures may vary qualitatively as well as quantitatively from one occupation to another but these dusts had stronger respiratory effects on the lungs of the farmers (Huy*et al.* 1991, Smid*et al.* 1992; Preller *et al.* 1995; Kullman 1998). Kouimintzis *et al.* 2007 and

Szczyrek*et al.* 2011 found a strong association between developing bronchitis, COPD and lung reduced force expiratory volume among livestock farmers who are exposed to high levels of organic dust in confined buildings. Dalphin*et al.* 1989 studied the prevalence of bronchitis and reduced respiratory function among livestock dairy farmers. He further concluded that dairy farmers are at a greater risk of developing respiratory disfunction. A large number of studies also supported and found a strong potential association between animal farming and non-malignant disorders, like asthma, chronic bronchitis organic dust toxic syndrome and hypersensitivity pneumonitis (Zejda*et al.* 1993; Omland 2002; Hoppin*et al.* 2003) as shown in table 2.

Table 2. Respiratory conditions due to occupational exposure

OCCUPATION	EXPOSURE	RESPIRATORY CONDITIONS
Dairy farmers	Organic dust Feed additives Thermophilic bacteria and fungi Fungi Microbial toxins Storage mites Irritant gases	Chronic Bronchitis, Organic dust toxic syndrome Asthma Allergic alveolitis (farmer's lung) Bronchiolitis Toxic pneumonitis (silo filler's lung) Rhinitis COPD (chronic obstructive pulmonary disease

Source: Merchant JA et al. Textbook on Clinical Occupational and Environmental Medicine. Eds. Rosenstock L, Cullen, 1994.

Various studies demonstrated that organic dusts present particularly ina Concentrated Animal Feeding Operations (CAFOs)i.e., is a system of farming which concentrates a large number of animals into a small space for maximum efficiency, may cause lung inflammation and assessed the respiratory health of the workers by testing dust mitigation strategies and further reported that organic dust and its components may be a deciding factor in understanding inflammatory response among livestock farmers who are exposed to the environment (Senthilselvan et al. 1997; Schnebergeret *al.* 2016 and Hawley *et al*. 2015) as shown in fig. 1.

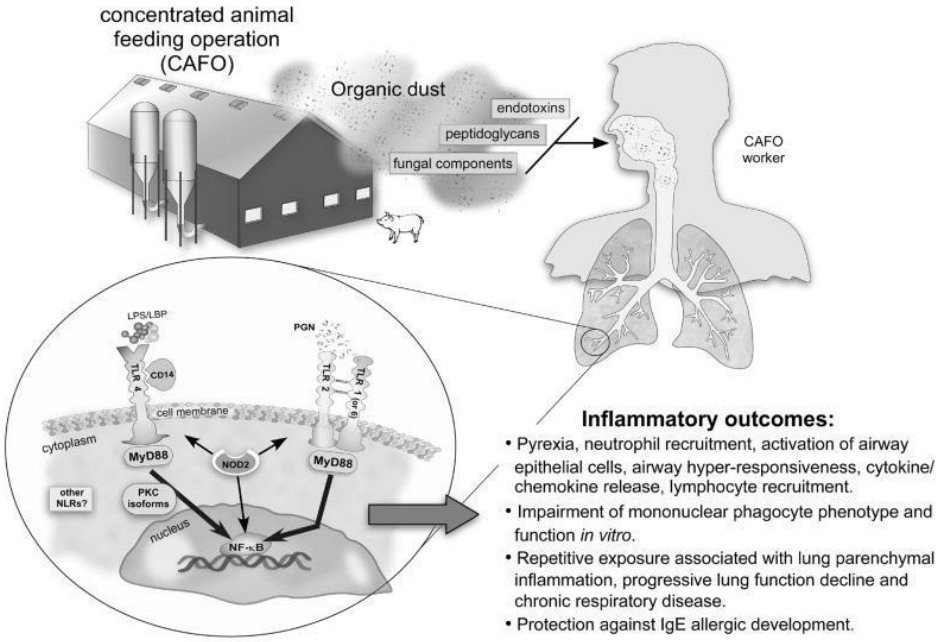

Fig.1: Poole, J. A., &Romberger, D. J. (2012). Immunological and inflammatory responses to organic dust in agriculture. Current opinion in allergy and clinical immunology. Diagrammatic presentation of the agents and immunologic and inflammatory consequences of organic dust exposure in the agriculture industry in large, concentrated animal feeding operations (CAFOs).

Exposure studies found a strong association between COPD, dust and endotoxins in confined livestock buildings and revealed the fact that livestock farmers had significant higher mortality rates due to their respiratory illness (Monso*et al.* 2004; Szczyrek*et al.* 2011). Van *et al.* 2016 and Sigsgaard*et al.* 2020 also recently investigated the impact of livestock farming on lung health of farmers in their epidemiological studies and reported the risk of developing chronic bronchitis and bronchial obstruction/COPD among livestock farmers. They concluded the higher prevalence of lower respiratory tract infections in the area with a high density of livestock farms. Dairy farm dusts are complex mixtures that contain both toxic and immunogenic compounds. Dust exposure is a major source of respiratory morbidity and mortality among agricultural workers (American Thoracic Society, 1998; Schenker, 2000; Linaker and Smedley, 2002; Cleave *et al.* 2009; Reynolds *et al.* 2013). A large number of studies indicated that dairy workers, in particular, have increased risks for **asthma, rhinitis, sinusitis, mucus membrane inflammation syndrome, bronchitis, chronic obstructive pulmonary disease (COPD), hypersensitivity pneumonitis, and organic dust toxic syndrome** (Kullman*et al.* 1998; Gainet*et al.* 2007; May *et al.* 2012; Reynolds *et al.* 2013).

Taluja, *et al.* 2019 also reported that occupational exposure of dust causes respiratory hazards to farm workers and concluded that dust adversely affects the respiratory function by deteriorating the lung function parameters. Similarly, number of exposure studies reported a range of respiratory and other symptoms including bronchitis, chest tightness, nasal congestion, organic dust toxic syndrome, occupational asthma, mucus membrane irritation, nausea, headache, mood changes, altered immunity among workers who are exposed to organic dust (Sahlander*et al.* 2012; Viegas*et al.* 2013; Iowa Concentrated Animal Feeding Operations Air Quality Study, 2018) and increased risks of lung cancer (Peters *et al.* 2012).

Various studies indicated health hazards and recognized a number of syndromes among workers in intensive livestock production (Donham *et al*.1995; Hartung and Schulz,2008). Organic dust toxic syndrome recognized in workers is predominantly a severe flu-like syndrome originally described in farmers and other persons who are occupationally exposed to dusty conditions. (Donham *et al.* 2002; Hartung and Schulz,2008) again reported the prevalence of ODTS ranges from 10 to 30% in workers, depending on the type of intensive animal production and use of facilities.Several studies have indicated that the prevalence of persistent restriction of airflow and pulmonary disordersare higher among dairy farmers than in the general population (Stoleski et al., 2015; Guillien et al., 2016; Marescaux et al., 2016; Guillien et al., 2019).As dairy farmers are exposed to high concentrations of organic dusts, this increased risk seems mainly driven by chronic exposure to these dusts (Basinas et al., 2014; Pfister et al., 2018).These findings suggest that presence of multiple microbial and non-microbial factors in OD can cause broad-range of health effects upon exposure which is a significant public health concern.

Mechanism involving lung inflammation

Cytokines play an important role in determining pulmonary diseases which includes **platelet-derived growth factor (PDGF),Interleukln-1 (IL-1), transforming growth factor-p (TGF-P), tumor necrosis factor-a (TNF-a), Insulin like growth factor I (IGF-I), Interleukin-& (IL-&) 1** (Kelley, 1990). Alterationsin cytokine production, secretion, and action represent determining forces in the destructive and inflammatory lung disorders as shown in fig. 2.

Recognition of micro-organisms is an important function of the innate and adaptive immunity and pattern recognition receptors (PRRs) recognize a variety of pathogen-associated molecular patterns (PAMPs) from viruses, bacteria, fungi and parasites (Takeda *et al.* 2003). Toll-like receptors (TLRs) comprise a group of PRRs which are expressed by most immune cells. When binding to PAMPs, immune responses including expression of proinflammatory cytokines and type I interferons (IFNs) are mediated through activation of the transcription factor **NF-kB and interferon regulatory factors (IRFs).** Currently, eleven TLRs have been identified in humans of which TLR2 and TLR4 are the most studied. Toll-like receptor 4 is activated by the endogenous molecules or danger signals released during tissue injuries in addition to bacterial endotoxins (Akira *et al.* 2006; Tsan and Gao 2004). Thus, TLR4 is the prototypical sensor of infection or injury that arranges the innate response via a sequential activation of both cell surface and endocytic signaling pathways (Ghosh *et al.* 2015). The increased expression of TLR4 has been associated with the lung dysfunction and elevated TLR4 subsequently activates nuclear factor kappa-light-chain-enhancer of activated B cells (NF-kB) which in turns directs the expression of various chemokines and pro-inflammatory cytokines including Interleukins-1β and tumor necrosis factor TNF-α (Strieter*et al*. 2002).

Lipopolysaccharides (LPS) is a major component of the outer membrane of gram-negative bacteria, (Sugiyama *et al.* 2008) is associated with the development and progression of various lung diseases characterized by chronic inflammatory conditions (Vernooy*et al.* 2002). Single LPS exposure is sufficient to rapidly recruit

neutrophils to the lung and to produce pro-inflammatory cytokines and chemokines (Deetz *et al.* 1997). The recognition of LPS is modulated by soluble factors, such as LPS binding protein and surfactant proteins that are present in airway lining fluid and influence the presentation of LPS to membrane-bound CD14 (Skerrett *et al.* 2004). Binding of LPS to CD14 triggers intracellular signaling that is mediated by Toll-like receptor 4 (TLR4) in association with a secreted cofactor, MD-2 (Akira *et al.* 2003). TLR2 recognizes PAMPs from Gram-positive bacteria like peptidoglycans (PGN) and lipoproteins and binds LPS from special bacteria strains and PAMPs from fungi (Takeda *et al.* 2003 and Akira *et al.* 2006). Zahringer*et al.* 2008 reported that TLR 2 is typically associated with the detection of peptidoglycans, lipoteichoic-acid, lipoproteins, lipopeptides and zymosan. (Oliveira-Nascimento *et al.* 2012; Kang *et al.* 2009; Oosting*et al.* 2014) further demonstrated the dimerization property of TLR2 with TLR1, TLR6 or TLR 10 which makes it to detect increased range of possible ligands. These studies have shown that TLR2 may be even more important than TLR4 in determining the response to these organic dusts. (Martin *et al.* 1996) also supported in their study that TLR2 may be more important than TLR4 in determining the response during organic dusts exposure. Whereas other studies supported the role of protein kinase C (PKC), TLR9 (Schnebergeret *al.* 2016); TLR2 (Poole *et al.* 2011); MyD88 (Bauer et al 2013) in several innate signaling pathways in response to organic dust exposure.

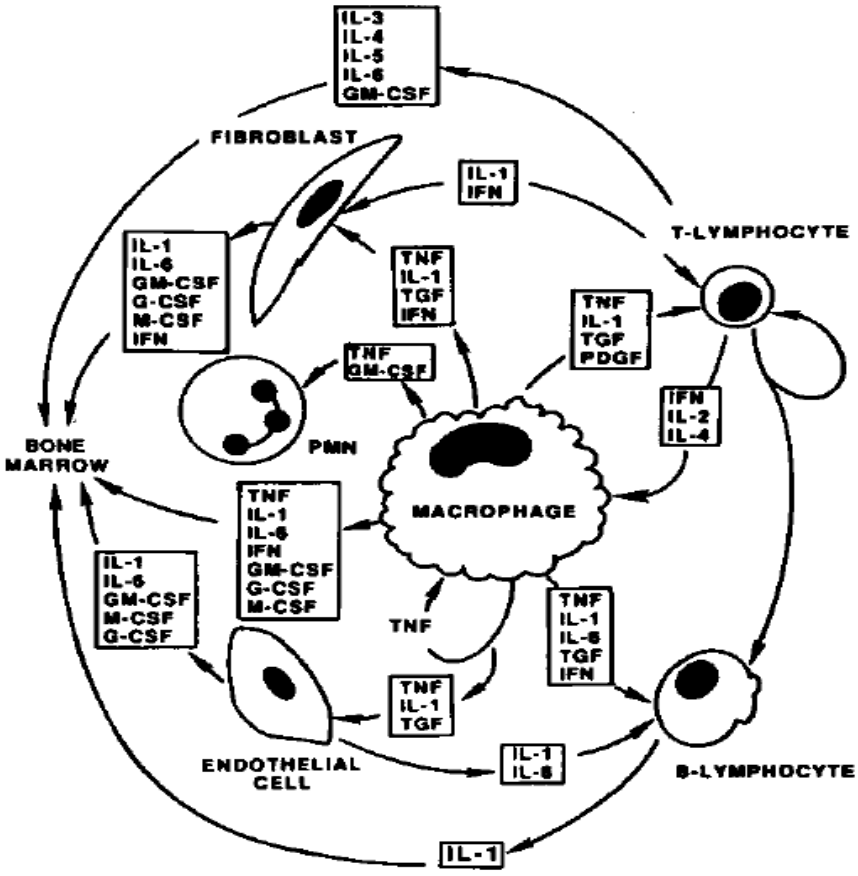

Figure 2. **Kelley, J. (1990). Cytokines of the lung. *Am Rev Respir Dis*, *141*(3), 765-788.**

Schematic showing multiple potential cellular interactions involving cytokines.

Interleukin-1β is a potent pro-inflammatory cytokine that is crucial for host-defense response to infection and injury (Lopez *et al.* 2011). Interleukin-1β, encoded by the IL-1β gene, has been associated with chronic inflammation and plays an important role in lung inflammatory diseases including lung cancer. Elevated levels of IL-1 proteins, in particular IL-1β greatly enhance the intensity of the inflammatory response (Bhat et al. 2014).(Zahringer*et al.* 2008) reported that TLR2 is associated with the detection of peptidoglycans, lipoteichoic acid, lipoproteins and zymosan. Senthilselvan*et al.* 2009 revealed the association of TLR4 gene and its ligand LPS as an important factor in

lung dysfunction after barn exposure in humans. (Sahlander*et al* 2010) studied association between T-helper (th) cell, cytokine *profile* and acute response to pro-inflammatory stimuli as markers. Whereas (Kang *et al.* 2009 and Oosting*et al.* 2014) reported that TLR2 can dimerize with TLR1, TLR6, TLR10 and can detect various range of possible ligands. Rombergeret *al.* 2015 discovered **proteolytic properties that can stimulate protease activated receptors (PARs) 1 and 2** in the bronchial epithelium and focused on the contribution of proteases to lung inflammation and pathways which contribute to the lung inflammatory response to dust exposure. These proteolytic properties of organic dusts require further investigations because some chemokines are also produced on cleavage although study suggested main effect is through PAR receptors.

Surfactant proteins (SP) are also important constituents of pulmonary defense and are a lipoprotein complex of phospholipids and apoproteins which is a complex critical component in lung immune host defense (Pastva et al. 2007).Surfactant, a lipoprotein. Pulmonary SPs are also involved in the pathophysiology of lung injury following exposure to pesticides (Gil et al. 2007).Although surfactants appear not to have been studied extensively in terms of organic dust whereas Schneberger et al. 2018 examined the role of the immune surfactant or collectin surfactant protein D (SP-D) in lungs induced prolonged exposure to organic barn dustsand concluded that organic barn dust can reduce lung SP-D, thus leaving workers potentially at risk for a host of pathogens.Sethi et al. 2017 also found SP-A and SP-D reductions in A549 lung cell linesexposed to hog barn dusts. This further suggests that some of the inflammatoryresponse generated in lungs to these dusts might beattributable to reductions in these immune surfactants.

In- vivo studies

Multiple researches identified organic dusts as a major problem in lung inflammation and have shown that organic dust exposure on human subjects and animals are helpful in accessing the pulmonary health of the occupational workers (Senthilselvan*et al.* 1997; Charavarymath*et al.* 2005; Schenebergeret *al.* 2016). Various animal models have been designed by the researchers which helped in understanding the molecular and cellular mechanisms of lung inflammation following exposures to livestock dust (Sethi *et al*. 2013 and Charavaryamath and singh 2006).

Charavaryamath*et al.* 2005 designed first rat model of human exposure to barn air which was mimicked human exposure of fulltime barn workers (8h/day, Monday to Friday) and found that single and multiple exposures to endotoxin rich-swine barn air induce lung inflammation characterized by infiltration of inflammatory cells, increased mucus positive-epithelial cells in addition to the presence of endotoxins, dust, ammonia, microorganisms, aeroallergens.

Charavarymath*et al.* 2006 supported that PIMMS cells are important because they have shown to produce both pro and anti-inflammatory cytokines to regulate lung inflammation.Further Gamage *et al.* 2007 demonstrated the role of pulmonary intravascular monocytes /macrophages (PIMMS) recruitment and their functions in lung inflammation induced following exposure to the barn air by using a rat model. Further interactions between PAR2 and TLR4 were also well demonstrated by Rallabahndi*et al.* 2008. Lundin and &Checkoway, 2009 reported altered TLR expression among livestock farmers who were probably exposed to organic agents and concluded that reduced TLR expression may be related to the increased prevalence of respiratory disorders among livestock farmers.

Sahlander et al. (2010) hypothesized that T-helper (Th) cell cytokine profile and acute response to pro-inflammatory stimuli as immune response among pig farmers and smokers. After in vivo exposure, altered TLR expression was only observed in controls and the ex vivo stimulations showed an attenuated response in farmers compared to the control group. The inflammatory systemic response to pro-inflammatory stimuli is altered in farmers probably because of adaptive mechanisms arising from chronic exposure to organic material and microbial compounds, have an increased number of inflammatory cells in peripheral blood and an increased proportion of circulating Th2- type lymphocytes which, among pig farmers, were positively related with the duration of work in pig confinement buildings.

Sethi *et al.* 2013 revealed a decrease in Clara cells and an increase in numbers of mucus producing goblet cells in the airway epithelium in exposed knockout TLR9 $^{-/-}$ animals after chronic barn exposure. Schneberger*et al.* 2016 reported that in TLR9 knockout mice no stronger responses has been detected as compared to TLR2 and TLR4 mice when exposed to the barn environment. Sethi *et al.* 2017 further demonstrated the role of innate inflammatory mechanism, especially TLR4 and TLR9 following exposure to dust and other pollutants in agriculture environments by using in vitro models and laboratory animals.

Nath *et al.* 2018 illustrated the association between the exacerbated inflammation upon persistent barn organic dust exposure, pathogenesis of lung inflammation and lung function decline. He investigated the inflammatory effects of Barn Dust Extracts on human lung epithelial **(BEAS2B)**

and macrophage (THP-1 monocyte derived) cell lines on a kinome array to determine phosphorylation events in the inflammatory signaling pathways. Further he concluded that workers exposed to persistent barn air are at occupational risk of developing a range of respiratory illnesses and there is a critical need to understand the mechanisms behind those illness.

Kaur and Sethi, 2020 concluded that multiple exposures of poultry barn air resulted in lung damage and damage is more severe when combined with LPS. Multiple exposures in combination with LPS significantly altered the mRNA and protein expression of TLR-4 and IL-1β. Expression of TLR4 and IL-1β showed a synergistic effect when combined with LPS.Woldeamanuel*et al*. 2020 and Soumagne*et al*. 2020 reviewed that dairy farmer could be exposed to various potentially hazardous exposures that can cause respiratory symptoms due to higher inflammatory markers such as such as TNFα, fibrinogen, IL-6 and CRP

In vitro studies

Poole et al. 2008 found that repetitive organic dust exposure significantly decreases markersof antigen presentation and host defense function in monocyte-derived macrophage (MDMs). Bacterial cell components appear to be driving these impaired responses**.Expression of HLA-DR, CD80, and CD86;** phagocytosis; and intracellular bacterial killing were significantly decreased with organic dust exposure (ODE)-challenged versus control MDMs. Responses were retained after marked depletion of endotoxin. PGN, LPS, and PGN plus LPS significantly reduced MDM surface marker expression and, except for LPS alone, also reduced phagocytosis. ODE-challenged MDMs had significantly diminished cytokine responses **(TNF-α, IL-6, and IL-10)** after repeat challenge with high-dose **ODE** and concluded that organic dust–induced macrophage dysfunction might be important in respiratory disease development.

Viegas*et al*. 2017 chosemacrophagesfor the in vitro assessment because they are known to be responsible for first-line protection and also for triggering the inflammatory response via secretion of signaling molecules.The cell viability and the inflammatory response, as measured by the production of pro-inflammatory cytokines tumor necrosis factor-α (TNFα) and interleukin-1 β (IL-1β), are determined in human macrophages derived from THP-1 monocytic cells. This study emphasizes the importance of measuring the organic dust/mixture effects in occupational settings and suggests that differences in the organic dust content may result in differences in health effects for exposed workers.

Nordgren and Charavaryamath in 2018 demonstrated the application of a kinome array to delineate key inflammatory signaling pathways activated upon swine barn dust extract SBDE exposure in vitro. They concluded that SBDE-mediated pro-inflammatory effects are predominantly due to the induction of neutrophilic chemokine IL-8. Differentially phosphorylated peptides implicated in IL-8 induction in BEAS2B cell line include, **TLR2, 4, 5, 7, 8, 9, PKC, MAP kinases (p38, JNK), inflammasomes (NLRP1, NLRP3), NF-κB and AP-1** due to persistent barn organic dust exposure which is a key contributor to the pathogenesis of lung inflammation and lung function decline.

Nordgren*et al*. 2013identified the role of mediators derived from polyunsaturated fatty acids exhibit anti-inflammatory, pre-resolving actions and tested the potential of one of these mediatorsi.e.,**maresin-1 (MaR1)**.As bronchial epithelial cells (BECs) playpivotal role in initiating organic dust-induced inflammation and they investigated the invitro effects of MaR1 on a human BEC cell line (BEAS-2B)in reducing organic dust-associated airway inflammation. Again Nordgren*et al*. 2015 supported the previous study that the specialized proresolving lipid **mediator maresin-1 (**MaR1) reduced proinflammatory cytokine release and **intracellular adhesion molecule-1 (ICAM-1)** expression in bronchial epithelial cells exposed to extracts of organic dust (DE) derived from swine confinement facilities in vitro. The data suggested that MaR1 might contribute to an effective strategy to reduce airway inflammatory diseases induced by agricultural-related organic dust environmental exposures.

Occupational lung diseases caused and aggravated by various organic and inorganic inhaled dust, fumes, and mist.Therefore, occupational history of livestock farmers should be considered when evaluating respiratory symptoms. The best way to treat OLDs as early as possible are prevention and early detection by controlling the working environment and conducting regular surveillance of workers (Lee, 2011).

There is an urgent need to improve knowledge on several topics, including 1) understanding thenature and pathophysiology of respiratory diseases, 2) diagnostic approaches, 3) disease behaviorand natural history, and 4) therapeuticapproaches. Key questions onpathophysiology includes geneticsusceptibility and both host andenvironmental factors. For diagnosticapproaches, important needs include thevalidation and standardization ofquestionnaires, BAL lymphocytosisthreshold, specific antibodies, andbiomarkers.In addition, new techniques

likegenomic classifiers and artificial intelligenceto improve diagnosis and prognosis need tobe assessed. For example;adiagnosis of hypersensitivity pneumonitis (HP) and distinguishing it from other forms of interstitial lung diseases.The diagnosis of HP relies on the integration of multiples domains such as clinical assessment of exposure, imaging, bronchoalveolar lavage lymphocytosis and histopathological findings. Among patients with fibrotic HP, the MUC5B (mucin 5B) promoter polymorphism is more prevalent than in the general population and is associated with shortened survival (Ley, 2017).Among sensitized individuals, the immune reaction after exposure to an antigen appears to consist of both humoral (i.e., antigen-specific IgG antibodies) and T-helper cell type 1 (Th1) cellular immune responses (Hisauchi-Kojima, 1999). These responses lead to a predominantly lymphocytic inflammatory pattern and granulomatous inflammation (Vasakova et al. 2019). Neutrophilic inflammationmay play a role early in the disease whereas impaired function of T regulatory cells may play a role in the exaggerated immune response(Pardo et al.2000). Similarly other pulmonary diseases can be detected by analyzing cytokines production, presence of IgG and IgE antibodies. Manyother antigens in organic dusts associated with these diseases have not been adequatelycharacterized and better understanding of the mechanisms by which thesematerials cause clinical disease is necessary.

CONCLUSION

From this review it has been concluded that pulmonary damage risk is associated with raising livestock animals due to organic dust exposure. Once the lung is damaged by organic dusts, regeneration of lung to normal state is almost impossible. Thus, prediction and early diagnosis of lung diseases are important and imperatively necessary. In spite of advanced technologies overall level of organic dust exposure of livestock workers is very high which poses a serious health threat. Exposure to organic dust and its health effects among workers have been investigated in numerous epidemiological and exposure-assessment studies during the last three decades.Further multiple components within the dust such as endotoxins, LPS and peptidoglycans bind to a wide variety of innate immune receptors but we still have no clear definition of the potential determinants of personal exposures in livestock farming environments. Work related respiratory diseases are major contributors to the global burden of respiratory diseases. This review is focused on the findings which suggested that livestock farmers are exposed to high levels of dust and endotoxin consistent with an increased risk of developing respiratory symptoms and diseases.

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