

AIRBORNE CONTAMINANTS AND FARMERS HEALTH IN SWINE FARMS WITH HIGH AND LOW PREVALENCE OF RESPIRATORY DISEASES IN PIGS

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Abstract: The main purpose of this study was to investigate the relationship between prevalence of respiratory disease in swine and respiratory health of swine farmers. Fourteen farms were selected based on clinical history and slaughtercheck evidence of respiratory problems in pigs. The farms were divided into two groups with either high (n = 7) or low (n = 7) prevalence of respiratory disease in pigs. Airborne dust, endotoxin and peptidoglycan were measured once in farrowing, gestation, nursery and finishing of each farm. Respiratory health of farmers in participating farms was evaluated by questionnaire and pulmonary function test. A mean of 71% of the pigs in high prevalence farms had pneumonic lesions at slaughter, compared with 7% in low prevalence farms. No significant relationship was found between prevalence of respiratory disease in pigs and airborne dust, endotoxin or peptidoglycan. More farmers in high prevalence farms reported chest tightness (p = 0.038). The percentage predicted FEF_{25%-75%} was lower (p = 0.046) in farmers working in high prevalence farms. Significant differences disappeared after adjusting for smoking status. Our study suggests that farmers working on farms with a high prevalence for respiratory disease in pigs may have more respiratory problems than farmers working in farms with low prevalence of such diseases.

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The major airborne contaminants in swine confinement buildings are dust, endotoxin, microorganisms and ammonia [9, 14]. Airborne dust in swine confinement buildings primarily originates from feed, dried fecal materials, skin debris, bacteria and molds [7, 10, 14, 25]. Recently, Martin *et al.* [25] suggested that in addition to the pigs, farm workers and environment (i.e. soil, water, feed, plants, etc.) are also significant sources of the microbial flora in airborne dust. This was concluded after microbiological evaluation of dust in swine farms indicated the presence of microorganisms of human and environmental origin. Biologically active agents in dust include endotoxin (a cell wall component of Gram-

negative bacteria), β -1,3-glucan (a cell wall component of molds) and peptidoglycan (a cell wall component of all bacteria) [9, 24].

Respiratory problems, such as occupational asthma and chronic bronchitis, are common in swine producers [9, 13, 15, 16, 19, 29]. The relationships between organic dust exposure and respiratory symptoms have been thoroughly investigated in swine producers around the world [4, 9, 11, 16, 28, 29, 35]. In particular, exposure to airborne endotoxin, even in the presence of relatively low dust concentrations, is considered a risk factor for respiratory problems and lung function changes in swine producers [10, 18, 29, 31, 33, 35].

Table 1. Summary of slaughtercheck data for farms with high and low respiratory problems in pigs.

Farm Type ^a	Respiratory lesions		
	Pneumonia	Pleuritis	Atrophic rhinitis
High (N = 7)	70.7% (53–87) ^b	22.7% (10–45)	29.1% (0–50)
Low (N = 7)	6.7% (0–17)	9.1% (0–20)	3% (0–12)

^aMean pigs examined/farm: High = 23 pigs examined, Low = 21 pigs examined; ^brange in %.

Similar to respiratory problems in swine producers, respiratory disease in swine cause important problems for the swine industry all over the world. In several studies, chronic pneumonia lesions and atrophic rhinitis have been observed at slaughter in 100% of swine herds tested and pleuritis in 70% of the herds [2, 6, 17, 27]. Pneumonia and rhinitis are estimated to cause annual losses of several hundred million dollars due to mortality and reduced weight gain [6]. Various infectious agents (viruses, bacteria, mycoplasmas) have been identified as primary etiological agents of swine respiratory disease. However, non-infectious airborne contaminants in swine confinement buildings might be critically important predisposing causes. In addition, the irritant and inflammatory nature of the environment in swine farms might impair the respiratory disease resistance of the pig [7, 20].

Few studies have investigated the relationship between respiratory problems of swine producers and their pigs, and airborne contaminants and respiratory problems in pigs. Bongers *et al.* [4] reported a significant association between altered pulmonary function of the farmers and frequency of lung disease in their pigs at slaughter. Donham [8] found high correlations between pneumonia in pigs at slaughter and total and respirable concentrations of airborne bacteria.

In this study, 14 farms were selected, based on prevalence and clinical history of respiratory diseases in pigs, location and willingness to participate. Prevalence was determined at slaughter and farms were assigned to a high or low prevalence group for respiratory disease. Airborne concentrations of total dust, endotoxin and peptidoglycan were measured and compared in both prevalence groups. In addition, the respiratory health of farmers working in the participating farms was evaluated by questionnaire and pulmonary function test (PFT) and was compared between prevalence groups.

MATERIALS AND METHODS

Farms. Seven farrow-to-finish swine herds, located in southern Wisconsin and northern Illinois, were selected for high prevalence of respiratory diseases in pigs based on clinical history and slaughtercheck evidence of chronic respiratory problems in pigs. Another 7 herds were selected for low prevalence of such diseases (Tab. 1). During an initial farm visit, the investigator recorded:

Table 2. Description of the selected farms.

No.	Farm size ^a	Hygiene ^b	AIAO ^c	Respiratory Lesions ^d			Prevalence ^e
				Pneumonia	Pleuritis	AR	
1.	600	2	1	87	23	33	H
2.	200	1	3	60	16	44	H
3.	200	1	1	5	5	0	L
4.	90	1	2	21	0	12	L
5.	200	1	1	54	33	0	H
6.	75	3	2	10	10	0	L
7.	100	2	3	65	9	50	H
8.	130	2	2	5	9	9	L
9.	400	2	1	10	10	0	L
10.	600	1	1	0	10	0	L
11.	75	1	2	0	10	0	L
12.	100	3	3	75	45	50	H
13.	450	2	2	75	30	50	H
14.	100	3	3	80	30	0	H

^aNumber of sows; ^bHygiene-Subjective score 1=high, 2=fair and 3=poor; ^cAIAO-All In/All Out - Subjective score 1=yes (i.e. AIAO in farrowing, nursery and finishing), 2=both (i.e. AIAO farrowing, continuous flow in nursery and/or finishing), 3=no (continuous flow in farrowing, nursery and finishing); ^d% of pigs with pneumonia, pleuritis or atrophic rhinitis (AR) lesions at slaughtercheck; ^eH=high prevalence of respiratory diseases in pigs, L= low.

1) herd size; 2) all-in all-out procedures - i.e. the simultaneous removal of all pigs from one room into another; 3) farm hygiene (Tab. 2). All-in all-out and hygiene procedures were subjectively scored on a scale from 1 to 3, with a lower mean score indicating better procedures. The farms used mostly confinement housing and mechanical ventilation systems. The study was conducted from January to March, 1995.

Environmental sampling. On each farm, one 1-hour total dust sample was collected on the same day in farrowing, gestation, nursery and finishing rooms with large volume dust samplers (LVS). Dust samplers were connected to a timer and sampled 10 minutes per hour over a 6 hour period. Flow rates of the LVS were calibrated and ranged between 324 and 354 l/min. Samples were obtained about 80 cm above the floor in the center of each room on PFTE (Teflon) filters with a Goretex support. The sampling time included one feeding period.

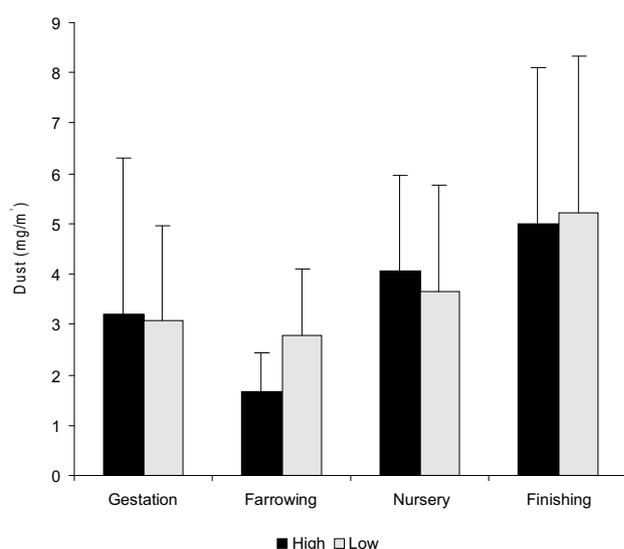
Analysis of the samples. Dust concentration was measured by gravimetric analysis of the filters pre-and post sampling and results were expressed as mg/m³. The filters were washed in 10 ml of pyrogen-free water for 1 hour while agitating and the washing solution was centrifuged (3000 rpm, 30 min). Supernatants were analyzed for endotoxin, using the turbidimetric Limulus

Table 3. Summary of selected airborne contaminants measured in different locations of the selected swine farms.

Location	Airborne contaminant		
	Dust (mg/m ³)	Endotoxin (ng/m ³)	PG (ng/m ³)
Farrowing	2.2 ± 1.2 ^{a, d} (0.6–5.1)	20.0 ± 12.8 (3.1–53.1)	469.2 ± 246.6 (163.2–1047.4)
Gestation	3.1 ± 2.5 (0.3–9.1)	40.1 ± 47.7 ^b (0.0–83.1)	325.9 ± 206.6 ^b (26.3–694.7)
Nursery	3.8 ± 1.9 ^b (0.3–6.7)	36.2 ± 24.1 ^c (3.1–93.0)	787.5 ± 501.4 ^b (257.9–1621.1)
Finishing	5.1 ± 2.9 (0.0–10.4)	37.9 ± 26.4 ^b (0.5–92.8)	365.6 ± 206.9 ^b (100.0–847.4)

^amean ± standard deviation (range), n = 14 ; ^bn = 13; ^cn = 12; ^dvalue significantly lower compared to finishing (p < 0.05); PG=peptidoglycan; 1 ng of endotoxin = 10 EU.

amoebocyte lysate (Limulus-ES II test, LAL ES-II test, Wako Pure Chemical Ltd, Japan), and for peptidoglycan and β-1,3-glucan, using the Silk Larvae Plasma reagent set (SLP, Wako). In the LAL ES-II, carboxymethylated curdlan is co-lyophilized with LAL, making this test specific for endotoxin. In the SLP test, peptidoglycan and β-1,3-glucan bind to a respective recognition protein, initiating the prophenoloxidase cascade system [34]. Prophenoloxidase is converted to phenoloxidase, which in turn catalyzes oxidation of 3, 4-dihydrophenylalanine, followed by the formation of melanin pigment. Increased absorbance due to melanin formation is read at 650 nm with a microplate reader. The concentration of peptidoglycan and β-1,3-glucan is obtained according to a standard curve. In this study, the SLP result primarily originated from peptidoglycan in the dust. The dust samples were extracted in pyrogen free water, which does not allow extraction of the water-insoluble β-1,3-glucan present in dust [30]. Endotoxin and peptidoglycan results

**Figure 1.** Dust concentrations (average ± standard deviation) in farms with high or low prevalence for respiratory diseases in pigs.

were expressed as ng/m³. Analysis of supernatant was carried out by M. Tsuchiya and A. Takaoka at Wako Pure Chemical in Japan.

Farmer's pulmonary status and function evaluation.

A trained technician visited each farm with a van equipped with a daily calibrated CPF-S/O spirometer for evaluation of pulmonary functions (Medical Graphics Corporation, St. Paul, MN). The technician instructed the workers and demonstrated the PFT technique according to standard procedures [3]. The farm workers performed the procedure during the work shift while seated and with the assistance of the technician. The best forced vital capacity (FVC), forced expiratory volume in one second (FEV₁) and forced expiratory flow during the middle half of an FEV maneuver (FEF_{25%-75%}) of 3 attempts were chosen for calculation of predicted values.

During the same farm visit, each worker also completed a modified American Thoracic Society (ATS) respiratory disease questionnaire. The questionnaire covered respiratory symptoms, work history, including agricultural and non-agricultural exposures, hours worked per day in swine facilities, and time spent on selected specific tasks.

Data analysis. Descriptive statistics for the environmental parameters were obtained with Quattro Pro for Windows spreadsheet program (Version 6). Multivariate analysis of environmental data against site and prevalence was generated with Statistical Analysis System (SAS Institute Inc., NC, USA). This model analyzed all response variables (dust, endotoxin and peptidoglycan) together and included 7 farms in each prevalence category and 4 sampling locations in each farm. Partial correlation coefficients examined relationships between dust, endotoxin and peptidoglycan in each sampling location, independent of prevalence.

Farmer data were analyzed with SAS and LogXact (CYTEL Software Corporation, MA, USA). Population characteristics were evaluated using descriptive statistics. The relationship between swine respiratory disease prevalence and presence of chronic respiratory disease in farmers was tested with a chi-square or Fisher's exact test, depending on the cell frequency. The relationship between symptoms, pulmonary function status, and behavioral variables such as smoking status, were examined using exact conditional logistic regressions given the small data set.

RESULTS

All-in all-out procedures were more common in herds with low prevalence for respiratory diseases in pigs as indicated by a lower mean score (=1.57), compared to the higher mean score in herds with high prevalence (=2.29) (Tab. 2). Similarly, farm hygiene in low prevalence herds was scored lower on average (=1.57) than in high prevalence herds (=2.00) (Tab. 2), suggesting better hygiene procedures in those herds.

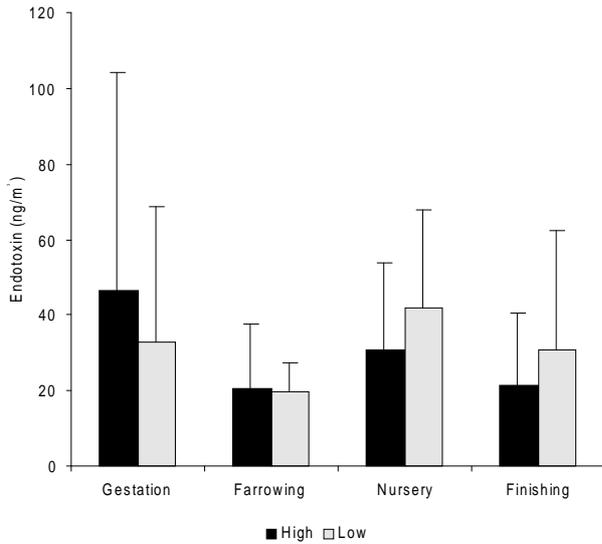


Figure 2. Endotoxin concentrations (average ± standard deviation) in farms with high or low prevalence for respiratory diseases in pigs.

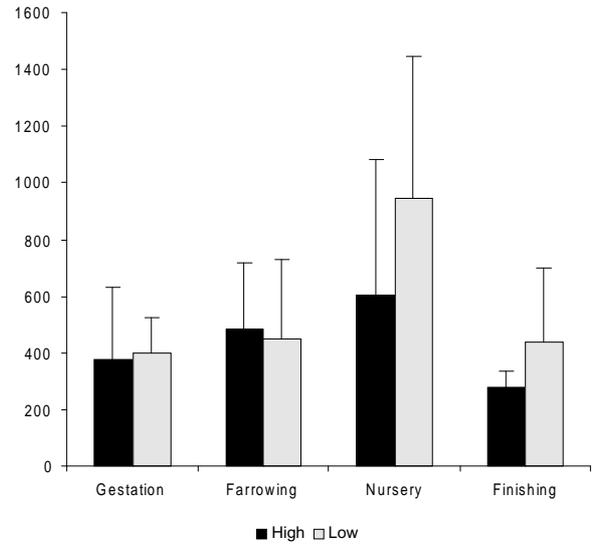


Figure 3. Peptidoglycan concentrations (average ± standard deviation) in farms with high or low prevalence for respiratory diseases in pigs.

Results of airborne contaminants are presented in Table 3 and Figures 1-3. Dust, endotoxin or peptidoglycan concentrations were not significantly different between prevalence groups. A significant difference was found between dust concentration in farrowing and finishing rooms (Tab. 3). Positive significant correlations were found between dust and peptidoglycan in gestation ($r = 0.652$, $p = 0.0156$) and finishing rooms ($r = 0.609$, $p = 0.0355$), and between peptidoglycan and endotoxin in gestation ($r = 0.766$, $p = 0.0023$) and farrowing rooms ($r = 0.682$, $p = 0.0102$).

The characteristics of participating farmers and their PFT are summarized in Tables 4 and 5. The farmers in both groups were white, had a high school diploma and were very similar in age, years farmed, number hours/day working in the barn, smoking history and respirator use. The average age of all farmers was 8 years younger than

farmers on average in Wisconsin. Consequently, their occupational experience was shorter. More farmers in the high prevalence farms reported symptoms, i.e. cough, phlegm, wheezing or chest tightness. A significantly ($p = 0.038$) higher percentage of farmers in high prevalence farms reported chest tightness in relation with working in the barns (Tab. 4). Pulmonary function results suggested relatively high FVC and FEV₁, regardless of farm type (Tab. 5). FEF_{25%-75%}, FEV₁/FVC and % FEV₁/FVC values were lower compared to those reported in other studies conducted during the winter in swine farms. The % predicted FEF_{25%-75%} was also significantly ($p = 0.046$) lower in farmers working in high prevalence farms. One farmer in the low prevalence group demonstrated marked decrease in pulmonary function for unknown reasons. However, removal of this case during data analysis did not change statistical significance.

Table 4. Descriptive statistics of the farmers working on farms with high or low prevalence of respiratory disease in pigs.

	Farm Type	
	High Prevalence	Low Prevalence
Number of farmers	15	16
Age	42.6 ± 12.6 ^a	43.3 ± 13.5
Years farmed	20.6 ± 13.3	22.5 ± 13.7
Hours/day in barn	5.5 ± 3.0	5.7 ± 2.5
Ever smoke	6 (40.0%)	6 (37.5%)
Respirator use	11 (73.3%)	10 (62.5%)
Farmers with symptoms	13 (86.7%)	11 (68.8%)
Cough	6 (40.0%)	7 (43.8%)
Pleghm	3 (20.0%)	5 (31.3%)
Wheezing	10 (66.7%)	7 (43.8%)
Chest tightness	12 (80.0%) ^b	7 (43.8%)

^amean ± standard deviation; ^bvalue significantly higher compared to low prevalence ($p < 0.05$)

Table 5. Pulmonary function test results of farmers working on farms with high or low prevalence for respiratory disease in pigs.

Pulmonary Function Test	Farm Type	
	High Prevalence (n = 15)	Low Prevalence (n = 16)
% Predicted FVC	101.7 ± 14.5 ^a	98.1 ± 15.8
% Predicted FEV ₁	93.3 ± 11.1	95.6 ± 17.5
% Predicted FEF _{25%-75%}	72.9 ± 19.4 ^b	88.4 ± 28.0
FEV ₁ /FVC	75.7 ± 7.1	80.0 ± 7.5
%FEV ₁ /%FVC	81.9 ± 1.3	82.3 ± 1.6

^amean ± standard deviation; ^bvalue significantly lower compared to low prevalence ($p < 0.05$); FVC - Forced Vital Capacity; FEV₁ - Forced Expiratory Volume in 1 second; FEF_{25%-75%} - Forced Expiratory Flow during the middle half of an FEV maneuver.

Table 6. Relationship between prevalence of respiratory disease in pigs and respiratory symptoms in farmers after adjusting for smoking status^a.

Respiratory symptom	p-value	Odds ratio	95% CI
Wheeze	0.447	2.69	(0.38, 23.84)
Cough	0.993	0.75	(0.12, 4.17)
Phlegm	0.756	0.56	(0.07, 3.63)
Chest tightness	0.100	5.68	(0.78, 58.89)
Respirator use	0.648	2.02	(0.31, 16.51)
Symptoms	0.545	2.76	(0.30, 39.34)

^a Smoking status was defined as: ever smoked cigarettes (>20 packs of cigarettes or 12 ounces of tobacco in a lifetime).

After adjusting for smoking, no significant relationship was detected between both prevalence groups and the odds of respiratory symptoms or pulmonary function tests in farmers (Tables 6 and 7).

DISCUSSION

The main objective of this paper was to compare airborne contaminants in swine farms and respiratory health of swine farmers with prevalence of respiratory disease in pigs. The study was conducted during the winter in farms with either high or low prevalence of respiratory disease in pigs. Overall, no differences were found in dust, endotoxin and peptidoglycan concentrations between the 2 prevalence groups. Possible explanations include the low number of farms, the variability between the farms within prevalence group and the collection of only one total dust sample in each farm area. Since our results originate from an area sampling rather than a personal sampling, the actual exposure of the worker might be slightly underestimated [35]. Such factors could interfere with the interpretation of the environmental data.

Total dust concentrations in the different farms were within previously reported ranges of 1.5 to 20 mg/m³ [5, 9, 10, 14, 23, 26, 35]. Farrowing units had the lowest average total dust concentration at 2.2 mg/m³ while finishing units had the highest at 5.1 mg/m³. Although the results of this study cannot be fully compared with others due to the different sampling techniques, the trend is in agreement with Donham *et al.* who reported increasing concentrations of total dust and a decreasing respirable dust fraction (particle size < 5 µm) from farrowing to finishing [14]. The average total dust concentrations in gestation, nursery and finishing were higher than 2.5 mg/m³, a concentration which has been associated previously with a significant cross-shift decrease in FEV₁ in swine farmers [10, 12, 29].

Total endotoxin concentrations in the different farm areas were at the lower end of previously reported ranges of 10 to 4100 ng/m³ (100 to 41,000 EU/m³) and were the lowest in farrowing units [9, 18, 21, 29, 35]. Overall, average endotoxin concentrations were slightly below 80 ng/m³ (800 EU/m³), which has been proposed by Donham

Table 7. Relationship between prevalence of respiratory disease in pigs and pulmonary function test in farmers after adjusting for smoking status^a.

Pulmonary function test	p-value	Odds ratio	SE estimate ^b
% Predicted FVC	0.552	3.35	5.66
% Predicted FEV ₁	0.703	-2.06	5.40
% Predicted FEF _{25%-75%}	0.105	-13.82	8.24
FEV ₁ /FVC	0.143	-3.82	2.54
%FEV ₁ / %FVC	0.587	-0.294	0.54

^aSmoking status was defined as: ever smoked cigarettes (>20 packs of cigarettes or 12 ounces of tobacco in a lifetime); ^b SE - standard error.

as a no-response threshold level in swine confinement [10, 29]. Airborne endotoxin has been found to play a more important role than dust in inducing symptoms and lung function changes in swine farmers [10, 18, 23, 29, 33, 35]. Higher endotoxin concentrations and cross-shift PFT changes have also been correlated in a study where farmers were followed for almost 2 years [31].

Bacterial contamination in swine confinement buildings primarily consists of Gram-positive bacteria and the highest concentrations are in farrowing and nursery facilities [1, 5, 7, 14, 25]. In this study, peptidoglycan, part of the cell wall of mainly Gram-positive bacteria, was measured as an indicator for bacterial contamination. The highest peptidoglycan concentration was also present in farrowing and nursery. In addition, peptidoglycan and endotoxin concentrations were correlated in gestation and farrowing. This is the first report which describes airborne peptidoglycan in swine confinement buildings. At this point, the significance of these peptidoglycan concentrations on respiratory health of pigs and farm workers is unknown. However, peptidoglycan can stimulate the immune response by activation of receptors on inflammatory cells, such as alveolar macrophages [22]. This could indicate a possible contributory role for airborne peptidoglycan in causing respiratory problems, although more studies are needed to confirm such hypothesis.

Even though concentrations of airborne contaminants in both prevalence groups were not different, significantly more farmers in high prevalence farms reported chest tightness and had lower % predicted FEF_{25%-75%} than farmers in low prevalence farms. However, the statistical significance disappeared after adjusting for smoking status because the number of farmers in each prevalence group became very small. This could explain why the relationship between farmers and swine respiratory health remains inconclusive. In addition, the respiratory health of farmers was only evaluated once during the work shift, which is in contrast with studies of over the work shift change [10, 29, 31]. Other frequently reported respiratory symptoms in both prevalence groups were cough, phlegm and wheezing. These results as well as PFT results were in agreement with those reported by others [4, 9, 10, 13, 15, 16, 18, 19, 31, 32, 35].

CONCLUSION

Our study suggests that farmers working in farms with a high prevalence for respiratory disease in pigs have more respiratory problems than farmers working in farms with low prevalence of such diseases. Unfortunately, the small number of farms and farmers and the variability between farms made it difficult to confirm the relationship between farmers health and swine health, and health and airborne contaminants. Our results are in agreement with other studies that swine farmers have a high prevalence of respiratory problems. This is also the first report about the presence of airborne peptidoglycan in the swine confinement buildings.

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REFERENCES

1. Attwood P, Brouwer R, Ruigewaard P, Versloot P, de Wit R, Heederik D, Boleij JSM: A study of the relationship between airborne contaminants and environmental factors in Dutch swine confinement buildings. *Am Ind Hyg Assoc J* 1987, **48**, 745-751.
2. Bahnson PB, Pointon AM, Dial DG, Marsh WE: Prevalence of lesions at slaughter in Minnesota swine herds. *12th Int Pig Vet Soc Congress, The Hague, The Netherlands*, 1992, 564-585.
3. Boehlecke B, Merchant JA: The use of pulmonary function testing and questionnaires as epidemiologic tools in the study of occupational lung disease. *Chest* 1981, **79**, 114S-121S.
4. Bongers P, Houthuijs D, Remijn B, Brouwer R, Biersteker K: Lung function and respiratory symptoms in pig farmers. *Br J Ind Med* 1987, **44**, 819-823.
5. Clark S, Rylander R, Larsson L: Airborne bacteria, endotoxin and fungi in dust in poultry and swine confinement buildings. *Am Ind Hyg Assoc J* 1983, **44**, 537-541.
6. Curtis SE, Bäckström L: Housing and environmental influences on production. **In:** Leman AD, Straw BE, Mengeling WL, D'Allaire S, Taylor DJ (Eds): *Diseases of Swine*, 884-900. Iowa State University Press, Ames, Iowa 1992.
7. Curtis SE, Drummond JG, Kelley KW, Grunloh DJ, Meares VJ, Norton HW, Jensen AH: Diurnal and annual fluctuations of aerial bacterial and dust levels in enclosed swine houses. *J Anim Sci* 1975, **41**, 1502-1511.
8. Donham KJ: Association of environmental air contaminants with disease and productivity in swine. *Am J Vet Res* 1991, **52**, 1723-1730.
9. Donham KJ: Swine confinement buildings. **In:** Rylander R, Jacobs RR (Eds): *Organic Dusts. Exposure, Effects, and Prevention*, 219-232. Lewis Publishers, Boca Raton 1994.
10. Donham KJ, Haglund P, Peterson Y, Rylander R, Belin L: Environmental and health studies of farm workers in Swedish swine confinement buildings. *Br J Ind Med* 1989, **46**, 31-37.
11. Donham KJ, Merchant JA, Lassise D, Popendorf W: Preventing respiratory disease in swine confinement workers: Intervention through applied epidemiology, education and consultation. *Am J Ind Med* 1990, **18**, 241-261.
12. Donham KJ, Reynolds S, Whitten P, Merchant J, Burmeister L, Popendorf W: Respiratory dysfunction associated with enclosed swine facilities: Dose-response investigations of pulmonary function and environmental exposures. *Am J Ind Med* 1995, **27**, 405-418.
13. Donham KJ, Rubino M, Thedell T, Kammermeyer J: Potential health hazards to agricultural workers in swine confinement buildings. *J Occup Med* 1977, **19**, 383-387.
14. Donham KJ, Scallon LJ, Popendorf W, Treuhaft MW, Roberts RC: Characterization of dust collected from swine confinement buildings. *Am Ind Hyg Assoc J* 1986, **47**, 404-410.
15. Donham KJ, Zavala DC, Merchant JA: Respiratory symptoms and lung function among workers in swine confinement buildings: A cross-sectional epidemiological study. *Arch Environ Health* 1984, **39**, 96-101.
16. Dosman JA, Graham BL, Hall D, Pahwa P, McDuffie HH, Lucewicz M, To T: Respiratory symptoms and alterations in pulmonary function tests in swine producers in Saskatchewan: Results of a survey of farmers. *J Occup Med* 1988, **30**, 715-720.
17. Elanco Products co: Largest slaughtercheck ever finds respiratory disease to be widespread. *Feedstuffs* 1985, **57**, 2.
18. Heederik D, Brouwer R, Biersteker K, Boleij JSM: Relationship of airborne endotoxin and bacteria levels in pig farms with the lung function and respiratory symptoms of farmers. *Int Arch Occup Environ Health* 1991, **62**, 595-601.
19. Holness DL, O'Brien EL, Sass-Kortsak A, Pilger C, Nethercott JR: Respiratory effects and dust exposure in hog confinement farming. *Am J Ind Med* 1987, **11**, 571-580.
20. Jolie R, Bäckström L, Olson L: Inflammatory changes in the respiratory tract of pigs induced by airborne contaminants present in swine confinement units. *14th Int Pig Vet Soc Congress, Bologna, Italy* 1996, 518.
21. Larsson K, Eklund A, Malmberg P, Belin L: Alterations in bronchoalveolar lavage fluid but not in lung function and bronchial responsiveness in swine confinement workers. *Chest* 1992, **101**, 767-774.
22. Malmberg P: Microorganisms. *Arbete och Halsa* 1991, **50**, 40-69.
23. Malmberg P, Larsson K: Acute exposure to swine dust causes bronchial hyperresponsiveness in healthy subjects. *Eur Respir J* 1993, **6**, 400-404.
24. Malmberg P, Rask-Andersen A: Organic dust toxic syndrome. *Semin Resp Med* 1993, **14**, 38-48.
25. Martin WT, Zhang Y, Willson P, Archer TP, Kinahan C, Barber EM: Bacterial and fungal flora of dust deposits in a pig building. *Occup Environ Med* 1996, **53**, 484-487.
26. Nicks B, Marlier D, Canart B: Air pollution levels in pig houses. *Livestock Environment IV ASAE Symposium, Coventry, England* 1993, 635-642.
27. Pijon C: Bacterial respiratory pathogens: What is their impact? *4th Annual Swine Disease Conference for Swine Practitioners, Ames, Iowa, USA* 1996, 45-47.
28. Preller L, Heederik D, Boleij JS, Vogelzang PFJ, Tielens MJ: Lung function and chronic symptoms of pig farmers: focus on exposure to endotoxins and ammonia and use of disinfectants. *Occup Environ Med* 1995, **52**, 654-660.
29. Reynolds S, Donham KJ, Whitten P, Merchant JA, Burmeister LF, Popendorf WJ: Longitudinal evaluation of dose-response relationships for environmental exposures and pulmonary function in swine production workers. *Am J Ind Med* 1996, **29**, 33-40.
30. Rylander R, Hsieh V, Courteuse C: The first case of sick building syndrome in Switzerland. *Indoor Environ* 1994, **3**, 159-162.
31. Schwartz DA, Donham KJ, Olenchock SA, Popendorf WJ, Van Fossen DS, Burmeister LF, Merchant JA: Determinants of longitudinal changes in spirometric function among swine confinement operators and farmers. *Am J Respir Crit Care Med* 1995, **151**, 47-53.
32. Schwartz DA, Landas SK, Lassise DL, Burmeister LF, Hunninghake GW, Merchant JA: Airway injury in swine confinement workers. *Ann Int Med* 1992, **116**, 630-635.
33. Smid T, Heederik D, Houba R, Quanjier PH: Dust- and endotoxin-related respiratory effects in the animal feed industry. *Am Rev Respir Dis* 1992, **146**, 1474-1479.
34. Tsuchiya M, Asahi N, Suzuoki F, Ashida M, Matsuura S: Detection of peptidoglycan and β -1,3-glucan with silkworm larvae plasma test. *FEMS Immunol Med Microbiol* 1996, **15**, 129-134.
35. Zejda JE, Barber EM, Dosman JA, Olenchock SA, McDuffie HH, Rhodes CS, Hurst TS: Respiratory health status in swine producers relates to endotoxin exposure in the presence of low dust levels. *J Occup Med* 1994, **36**, 49-56.