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CASE STUDY

Occupational asthma in newly employed workers in intensive swine confinement facilities

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Occupational asthma in newly employed workers in intensive swine confinement facilities. J.A. Dosman, J.A. Lawson, S.P. Kirychuk, Y. Cormier, J. Biem, N. Koehncke. ©ERS Journals Ltd 2004.

ABSTRACT: Respiratory symptoms, reductions in pulmonary function and increased bronchial responsiveness have been described in exposed workers and in naïve volunteers exposed to intensive swine production facilities. Typically, this occurs in persons who have been employed for a long duration or in previously unexposed, naïve volunteers.

The current authors describe four cases, all female, who developed acute onset of wheezing and cough suggestive of asthma within weeks of commencing full-time employment in intensive swine production facilities.

None of the workers were aware of any previous asthma, allergies or hay fever. All four employees reported improvement of symptoms on cessation of work in the facilities and consequent withdrawal from exposure. However, when seen at the respiratory clinic, cases 1 and 3 continued to be either mildly symptomatic or were taking medications with continued borderline airways responsiveness, as measured by methacholine challenge test up to 4 and 5 months, respectively, following work cessation. Case 2 continued to have symptoms for $\geqslant$3 months after work cessation. Only case 1, however, was seen at repeated visits in the respiratory clinic. One worker participated in a work re-entry trial and experienced profound coughing and chest tightness within an hour of entry, after which, the trial had to be terminated. Provocative concentration causing a 20% fall in forced expiratory volume in one second (PC_{20}) measured 5 h later was lower than pre-trial PC_{20}. No acute exposure event was recorded in the workers prior to the onset of symptoms.

To the current authors' knowledge, this is the first report of occupational asthma occurring in newly employed full-time intensive swine production workers after a short-term exposure and should raise awareness that previously unexposed workers may be at risk of developing what would appear to be long-term asthma after relatively short-term exposure.

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Respiratory symptoms [1–3], reductions in mean and across shift lung-function values [1, 4–6] and increased bronchial responsiveness [3, 7–14] have been described in exposed workers and in naïve volunteers exposed to intensive swine production facilities. In addition to this, SUNDBLAD *et al.* [13] demonstrated that exhaled nitric oxide (NO) increased following exposure only when a half mask was not worn, despite both groups (those wearing and those not wearing a mask) showing increased bronchial responsiveness, suggesting that the two outcome measures reflect different aspects of airway inflammation. O'SULLIVAN *et al.* [14] demonstrated that cysteinyl leukotrienes and other mast cell mediators are related to the development of increased bronchial responsiveness following exposure to a swine facility. Excess longitudinal decline in lung function has been reported in persons working in swine confinement facilities [15]. Swine confinement facilities are known to contain a number of pollutants associated with respiratory manifestations, including ammonia, hydrogen sulphide, dust and endotoxin [2, 16, 17]. The new large production facilities with full-time employees (*i.e.* $\geqslant$8 h *q.d.*) have exposure to substances at similar or greater levels than those described for older, smaller family-operated facilities [18]. Asthma has been reported in swine farmers, but after long-term exposure [2, 19]. A case of allergic occupational asthma from pig urine has been reported, but this case was highly atopic and eczematous and was exposed through agricultural training, not from working in a swine confinement facility [20].

In this report, the current authors describe the short-term onset of asthma in four females working in swine confinement facilities. To the current authors' knowledge, this is the first report of occupational asthma occurring where onset was shortly after commencing employment in this industry.

Case reports

Case 1

A 29-yr-old Caucasian female was referred to the respiratory clinic (Royal University Hospital, Saskatoon, Canada) 6 months after commencing full-time (~8 h *q.d.*) work at a swine confinement facility (fig. 1, table 1). Her duties included farrowing and feeding. She began having chest tightness

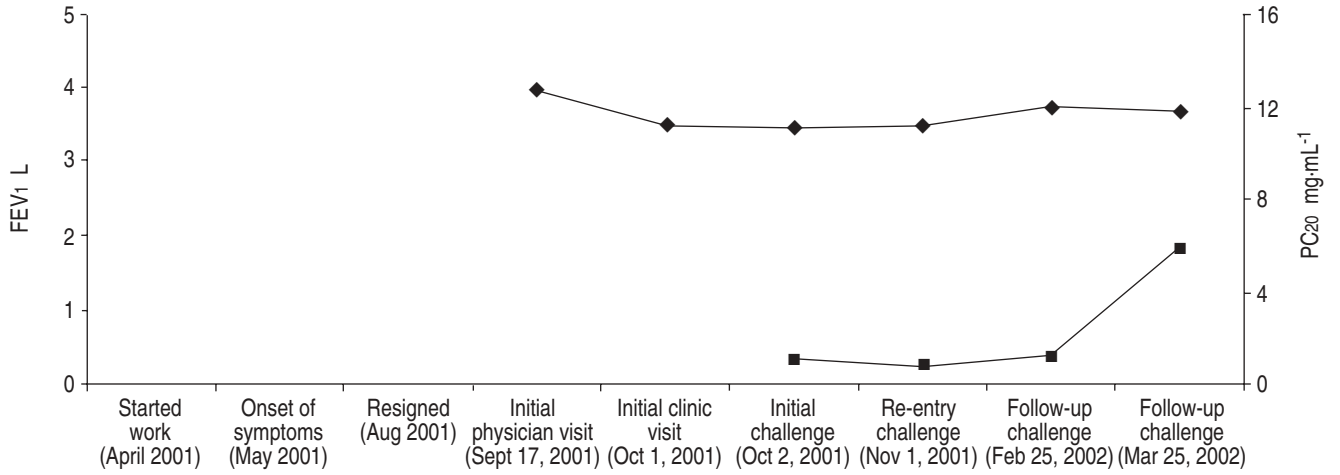

Fig. 1. – Timeline, forced expiratory volume in one second (FEV_1; ◆) and provocative concentration causing a 20% fall in FEV_1 (PC_{20}; ■) results for case 1.

~6 weeks after commencing employment and found that after working for 5–7 consecutive days she had chest tightness and wheezing. Typically, the patient would begin to cough frequently until emesis within 2 h after starting work in the morning. In the initial months, her symptoms improved on days off. After working for 4.5 months, the symptoms of chest tightness, cough and wheeze were so persistent and severe that she could no longer continue to work in the barn and she resigned from employment. When seen in the respiratory clinic 6 months after commencing work and 1.5 months after resigning from the swine production unit, the patient continued to have symptoms of chest tightness, wheeze and productive cough. She was treated with 125 μg fluticasone propionate *b.i.d.* (GlaxoWellcome Inc., Mississauga, Ontario, Canada) by metered dose inhaler (MDI).

The patient had no previous history of asthma or known allergy. Although she had previously worked on her parents' grain farm without difficulty, there was no other history of previous agricultural occupations or hazardous occupational exposures. She had a 14 pack-yr history and had been smoking since age 15 yrs, but had reduced this to 10 cigarettes *q.d.* by the time of the visit.

Examination revealed coarse rhonchi on forced expiration bilaterally. Chest radiography was clear. Sinus radiography showed minimal mucosal thickening in the right maxillary and ethnoid sinuses. Pulmonary function measures of forced expiratory volume in one second (FEV_1; 3.48 L), forced vital capacity (FVC; 4.36 L) and FEV_1/FVC ratio (0.80) were normal and FEV_1 improved by 10% to 3.83 L after 200 μg of inhaled salbutamol (Apotex Inc., Toronto, Ontario, Canada). Allergy testing at the initial physician visit showed positive reactions ranging from 3–9 mm weal size for various tree, weed and grass mixes as well as alfalfa. Testing was completed on the right forearm. Assessment of reaction magnitude was carried out by measuring the weal after 10 min. Other allergens tested included: feather; moulds (mix, hormodendrum, alternaria, aspergillus, penicillium, fusarium, mucor, helminthosporium); yeasts (brewer's, baker's); housedust mites; grains; histamine; and cat, dog, horse and hog hair. Methacholine challenge [21] revealed a provocative concentration causing a 20% fall in FEV_1 (PC_{20}) of 1.03 $mg \cdot mL^{-1}$.

One month after the initial clinic visit, 2.5 months after work cessation, case 1 attempted a re-entry challenge into the swine facility. This resulted in marked cough and wheeze

Table 1. – Age, employment and health history information for the four cases

	Case 1	Case 2	Case 3	Case 4
Age yrs	29	38	44	39
Occupational exposure time months	4.5	6	27	~48
Time from onset of work to onset of symptoms months	1.5	1	<6	<12
FEV_1 L	Sep 2001: 3.96 Oct 2001: 3.48 Oct 2001: 3.45 Nov 2001: 3.51 Feb 2002: 3.73 Mar 2002: 3.69	Dec 2001: 2.60 Jan 2002: 2.41 Mar 2002: 2.42	May 2003: 2.43	Mar 2003: 2.77
PC_{20} $mg \cdot mL^{-1}$	Oct 2001: 1.03 Nov 2001: 0.74 Feb 2002: 1.23 Mar 2002: 5.90	Mar 2002: 3.43	May 2003: 1.66	Mar 2003: >32
Skin-prick test reactivity weal size mm	Tree mix: >3 Weed mix: >3 Grass mix: >3 Alfalfa: >3	Horse: >3 Cat: 1–2 Swine: 1–2	House dust mite: 1–2 House dust: 1–2 Grain dust: 1–2	None
Smoking status	Current smoker	Current smoker	Never-smoker	Ex-smoker

Data are presented as n, unless otherwise stated. FEV_1: forced expiratory volume in one second; PC_{20}: provocative concentration causing a 20% fall in FEV_1.

within 0.5 h of entering the barn and the trial was terminated after 1 h due to the acute symptoms. Methacholine challenge, conducted ~5 h after cessation of exposure following re-entry, showed PC20 of 0.74 mg·mL^{-1}. Approximately 4 months later, when the worker was no longer on inhaled steroid therapy and was only mildly symptomatic, repeat methacholine challenge showed a PC20 of 1.23 mg·mL^{-1}. A final methacholine challenge conducted in March 2002, which was 7.5 months after stopping work in the swine facility, showed a PC20 of 5.9 mg·mL^{-1}.

Case 2

A second case, a 38-yr-old Caucasian female, was referred to the respiratory clinic 8 months after commencing full-time employment in an intensive swine production facility, where her tasks involved feeding pigs and handling feed (table 1). The patient began having symptoms of nasal stuffiness, cough and wheeze ~1 month after commencing employment. Symptoms were worse during the workday and improved on days off. After 5 months of work, she was diagnosed as having bronchitis. Shortly after this, the patient was told that she had pneumonia. This required 1 month off work, during which time her symptoms improved. Almost immediately after returning to work, she developed severe cough and wheeze in the barn, which increased over ~4 weeks, after which she resigned from work because of her symptoms. The patient's cough and wheeze improved to some extent in the ensuing month. When first seen in the respiratory clinic, 2 months after work cessation, she still wheezed. At this time, the patient was being treated with 250 μg fluticasone propionate MDI *b.i.d.*

The patient had no previous history of asthma or known allergy, although she had a history of sinusitis. At the time of the visit, she lived on a farm and had horses. There was no previous history of other agricultural occupations or hazardous occupational exposures. She had a 20 pack-yr history of smoking and continued to smoke 20 cigarettes *q.d.*

Chest radiography showed mild airways thickening. Allergy skin-prick tests (extracts from Western Allergy Services, Mississauga, Ontario, Canada), using the same method as case 1, showed a positive reaction to horse (>3 mm) and borderline (1–2 mm reaction) to cat and swine hair. Other allergens tested included: moulds (aspergillus, hemlinthosporium, cladosporium, alternaria); foods (egg, milk, peanut, shellfish); house dust mite; dusts (house, grain wheat); feather; animals (dog, cattle); trees (elder, birch, poplar, willow and mixed trees and grasses); and histamine. Pulmonary function measures of FEV1 (2.41 L), FVC (3.43 L), and FEV1/FVC ratio (0.70) were normal. Three months after work cessation, she continued to wheeze and required inhaled 250 μg fluticasone propionate *q.d.* along with inhaled salbutamol *b.i.d.* A methacholine challenge conducted 3 months after work cessation revealed a PC20 of 3.43 mg·mL^{-1}.

Case 3

The third case was a 44-yr-old Caucasian female (table 1). She began work in a swine facility in October 1999 where her duties included shipping, cleaning and working in the nursery following weaning. Symptoms, including severe coughing, frequently until she felt like vomiting, would occur when there was a large amount of dust in the barn. In the spring of 2000 and 2001, she developed bronchitis. A third bout of bronchitis was experienced in December 2002, which also included symptoms of cough, wheeze and chest tightness. Treatment lasted 2–3 weeks before symptoms began to subside, at which point, she was advised not to return to work. She has since remained on fluticasone propionate.

Case 3 had no previous history of asthma or known allergy. The patient had grown up on a farm and both she and her husband are farmers where she has helped periodically with grain. However, she had not previously had respiratory symptoms. There was no previous history of other hazardous occupational exposures. She was a lifetime never-smoker.

Chest radiography was unremarkable. Allergy skin-prick tests, using the same method as case 1, showed a borderline positive reaction to house dust mite, house dust and grain dust (<3 mm). Testing for hog hair was negative. Other allergens tested were the same as for case 2 and were negative. Pulmonary function measures of FEV1 (2.43 L), FVC (3.23 L) and FEV1/FVC ratio (0.75) were normal. Forced mid-expiratory flow was 61% of reference at 1.95 L·s^{-1}. A methacholine challenge conducted about 5.5 months after work cessation revealed a PC20 of 1.66 mg·mL^{-1}.

Case 4

Case 4 was a 39-yr-old female who began working in a swine facility in 1998 (table 1). After beginning to work in the facility, she began to have symptoms of cough, itchy eyes and sinus trouble. These gradually subsided, but became worse and within 1 yr of commencing work at the swine facility she developed an early morning cough. The cough was worse when she was in the barn and at night after work, but improved at weekends and during extended lengths of time away from work. The patient's symptoms gradually increased until she was placed on 250 μg inhaled fluticasone propionate *b.i.d.* and inhaled salbutamol as required in October 2002. Following one extended stay away from work, she wheezed heavily at night which interrupted her sleep. In November 2002, she ceased to work at the barn. Within a few days, her symptoms improved and she stopped taking the medicines. She had no previous history of asthma or known allergy. She is an ex-smoker with a ~24 pack-yr history.

Chest radiography was unremarkable. Allergy skin-prick tests, using the same method as case 1, showed negative reactions to all allergens including swine hair. Other allergens tested were the same as for case 2. Pulmonary function measures of FEV1 (2.77 L), FVC (3.36 L), and FEV1/FVC ratio (0.82) were normal. A methacholine challenge conducted ~5.5 months after work cessation revealed a PC20 of >32 mg·mL^{-1}.

Discussion

The current authors present four cases, all female, who developed respiratory symptoms after a relatively short exposure in swine confinement facilities, necessitating withdrawal from the workplace. Case 1 exhibited increased bronchial responsiveness that reverted towards borderline bronchial hyperresponsiveness after exposure withdrawal. The diagnostic criteria of asthma in these cases is consistent with occupational asthma, according to American College of Chest Physicians guidelines which include: asthma diagnosis; onset after entering the workplace; association between asthma symptoms and work; and either work-related changes in FEV1 or peak expiratory flow rate, work-related changes in bronchial responsiveness, positive response to a specific inhalation challenge test or onset of asthma with a clear association and a symptomatic exposure to an irritant agent

in the workplace [22]. Case 4 is the exception with normal pulmonary function and bronchial responsiveness. However, case 4 experienced severe symptoms requiring medication and methacholine challenge was conducted several months after exposure cessation. Although one limitation of the current authors′ report is the lack of longitudinal data, especially with regard to the pre-employment period and objective measures, on the basis of respiratory symptoms and increased airway hyperresponsiveness these cases appear to demonstrate a scenario that is compatible with occupational asthma. However, with the exception of case 1, the current authors′ conclusions are still based on case histories and report of symptoms.

Whilst the current authors do not have dust, endotoxin or ammonia measurements from the barns where these cases worked, these levels have been previously measured in other swine confinement facilities in Saskatchewan [23]. In these facilities, the mean±SD values of total dust were 2.9±0.9 $mg \cdot m^{-3}$, mean values of endotoxin were ≈11,400 $EU \cdot m^{-3}$±0.9 $mg \cdot m^{-3}$ and mean±SD values of ammonia were 11.3±4.2 ppm. Despite the case subjects working in newer barns, the current authors have no reason to believe that the exposures for these cases were substantially different than those previously described, as newer facilities have been shown to have at least the same levels of exposure as the older facilities [18].

Reactive airways dysfunction syndrome (RADS) after an acute swine barn exposure episode [24] and occupational asthma related to long-term swine barn exposures [2] have been documented. The respiratory complex of the cases the current authors reported appear to more closely resemble occupational asthma than RADS, as there is no history of acute exposure to toxic fumes or gas nor do the symptoms occur abruptly, which is characteristic of RADS [25]. Rather, there is progressive increase in symptoms and presence of nonspecific bronchial hyperresponsiveness [22], both of which appear to be work-related after a short-term exposure.

In the spectrum of occupational asthma, BROOKS *et al.* [26] characterise "not-so-sudden onset" asthma that develops within 1 day to 4 months of exposure to irritants. This is different from allergic occupational asthma, which occurs after a latent period of ~4 months and results from an exposure known to cause allergic-type asthma. Although the current authors cannot entirely rule out allergic occupational asthma, especially considering case 2 exhibited a borderline reaction to swine, it is believed that the cases are consistent with the BROOKS *et al.* [26] theory of not-so-sudden onset irritant-induced asthma, given the temporal trends. As such, these would be the first reported cases, to the current authors′ knowledge, of not-so-sudden onset asthma after occupational exposure in intensive swine confinement operations. It is possible that not-so-sudden onset occupational asthma may occur with short exposure periods in this occupational population, but that affected individuals may leave the industry, this being identified in the industry as "healthy worker effect" [27]. Certainly, exposures of volunteers to swine dust results in evidence for inflammatory response reflected by increased bronchial responsiveness to methacholine [14]. These effects are not totally eliminated by the use of personal protective devices, despite showing that exhaled NO is not increased following swine dust exposure when wearing a half mask [13].

Three of these cases were known to be smokers. In previous studies on swine-facility workers, a potential interaction between smoking and pig farming has been hypothesised [6, 28, 29]. Thus, the current cases may have been affected from a combined effect of smoking and exposures in a swine facility. Despite this, work in swine facilities has been independently associated with respiratory symptoms after accounting for smoking [3, 30, 31].

Although apparent occupational asthma or asthma-like syndrome has been associated with long-term exposure to swine confinement facilities [2, 19] and with acute exposure [24], the four cases that the current authors reported suggest that some persons may be vulnerable to the development of not-so sudden onset asthma or asthma-like syndrome after exposure to the swine barn environment, even following short-term exposure. Two of the four cases (cases 1 and 2) exhibited positive reactions on skin-prick tests to at least one allergen, and case 3 showed borderline positive atopic reactions. Despite none showing a definitive response to swine and no reported history of allergy, the potential for the cases to be allergic is presently based on the skin-prick tests. This supports the findings of BROOKS *et al.* [26], where it may be that allergy status is a potential risk factor for the development of not-so-sudden onset occupational asthma.

Increased bronchial hyperresponsiveness has been shown to occur in naïve subjects with little farm experience and no asthma or allergies [12]. While exposure levels in the swine barns where the current cases worked were not measured, it could be that the composition or level of exposures did not lead to acute reactions; however, continued exposure for a short period of time (weeks) can not only increase bronchial responsiveness, but occupational asthma can also develop.

All of these cases had symptoms within weeks of beginning exposure, but continued working in that environment. They also had asthma that persisted after exposure cessation. The persistence of occupational asthma after removal from work has been described in other industries [32]. The most effective way to prevent long-term asthma is early recognition and removal from the causative environment. If these cases had been withdrawn earlier it is possible that the persistence of the asthma after the cessation of exposure may have been prevented or shortened. These cases demonstrate the importance of awareness of potential respiratory problems in the swine industry and suggest that the worker and physician should act decisively when respiratory symptoms are present.

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