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EXPOSURE AND RESPIRATORY HEALTH IN FARMING IN TEMPERATE ZONES – A REVIEW OF THE LITERATURE

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Abstract: To review studies in farming populations from temperate zones focusing on: (1) exposure to dust, bacteria, moulds, endotoxin, and ammonia, (2) sensitisation to common airborne allergens, (3) prevalence, incidence and risk factors of chronic bronchitis, asthma and bronchial hyperresponsiveness, and (4) measurements of lung function. Working in animal housings can be associated with exposure to organic dust, bacteria, moulds, endotoxin, and ammonia in concentrations that can induce cellular and immunological responses and result in respiratory diseases. Working in poultry housing might be associated with higher exposures to dust, bacteria, and ammonia than in swine and cow housings, and endotoxin exposure seems to be higher in North America than in Europe. Working exposure might influence the domestic area on farms, and there might be a protective effect of being raised on a farm regarding sensitisation and allergic diseases. Sensitisation to mites seems to be the most prevalent of the common inhalant allergens. Chronic bronchitis is frequent and data suggests that it is work related in farmers. Findings concerning asthma are less uniform, and data regarding bronchial hyperresponsiveness are too sparse and inconsistent to evaluate the effect on farming. Several risk factors have been described, and age is shared for all three clinical manifestations, while male gender, atopy, smoking, pig farming, and animal production are common risk factors for chronic bronchitis and asthma. FEV_1, and FEV_1/FVC seems to be reduced in farmers, and longitudinal studies indicate an increased annual loss in FEV_1 in farmers, especially in pig farmers. The increased annual decline has been associated with lung function, bronchial hyperresponsiveness, smoking, automatic dry feeding systems, and endotoxin. Despite studies with methodological weaknesses, heterogenity in sampling times, measurement techniques, equipment, and diagnostic criteria, the review has revealed that the exposure to organic dust in farming can be substantial and might lead to respiratory diseases and increased annual loss in lung function. Working exposure seems to influence the domestic area in farms, and being raised on a farm might have a protective effect regarding sensitisation and allergic diseases.

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INTRODUCTION

Background. Working in agriculture represents a major occupational hazard for respiratory disease.

The predominant exposure to fumes and dust from farming in temperate zones occurs during work in animal buildings and barns. Dust, bacteria, moulds, endotoxin and ammonia are central elements in the daily exposure and these substances have often been measured and related to respiratory health. CO_2 is less frequently measured although concentrations have been found that might influence respiratory health (> 5000 ppm) especially in wintertime.

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Table 1. Total dust stationary sampling in mg/m^3.

country	housing	N	mean	range	reference
CAN	swine	54	2.93	1.71–5.02	122
NL	swine	175	4.01	0.47–23.48	37
US	swine	45	4.3		24
CAN	swine	8	3.54	2.20–5.63	14
FIN	swine	6	8.5	6.5–11.3	65
UK	swine	75	1.87		102
NL	swine	48	2.43		102
DK	swine	64	2.76		102
D	swine	68	1.95		102
FIN	cow	5	0.36–0.69		109
D	cow	211	0.74	0.007–6.5	62
FIN	cow	10	1.0	0.1–1.3	65
UK	cow	36	0.22		102
NL	cow	64	0.30		102
DK	cow	63	0.39		102
D	cow	68	0.65		102
FIN	poultry	11	6.0	2.7–13.1	65

1011 measurements.

The lowest mean value was 0.22 mg/m^3 and the highest was 8.5 mg/m^3, (range 0.007–23.48 mg/m^3). The measurements in Table 1 might indicate a higher exposure in swine houses (mean 1.87–8.5 mg/m^3, range 0.47–23.48 mg/m^3) than exposure in cow houses (mean 0.22–1.0 mg/m^3, range 0.007 B6.5 mg/m^3). Exposure assessment in poultry housing are too sparse to allow any comparison with exposure in pig- and cow houses.

Table 2. Respirable dust stationary sampling in mg/m^3.

country	housing	N	mean	range	reference
CAN	swine	54	0.13	0.05–0.32	122
US	swine	38	0.3		24
UK	swine	75	0.24		102
NL	swine	48	0.25		102
DK	swine	64	0.26		102
D	swine	68	0.18		102
UK	cow	35	0.15		102
NL	cow	62	0.09		102
DK	cow	64	0.04		102
D	cow	68	0.05		102
US	cow	217	0.07	0.007–8.03	62
UK	poultry	43	0.51		102
NL	poultry	49	0.58		102
DK	poultry	32	0.64		102
D	poultry	32	0.19		102

949 measurements.

Lowest mean value was 0.04 mg/m^3 and the highest was 0.64 mg/m^3. The range was given only for two set of measurements and was found between 0.007 mg/m^3 and 8.03 mg/m^3. Exposure in poultry housing (mean 0.64 to 0.19 mg/m^3) might be higher than in swine housing (mean 0.30 to 0.18 mg/m^3) and even lower in cow housing (mean 0.15 to 0.04 mg/m^3).

Exposure to the highly toxic gas hydrogen sulphide can cause sudden death if presented under anaerobic circumstances, but the gas represents hardly any risk as an irritant to the lungs in concentrations that might be measured in animal houses in modern farming under aerobic circumstances. Besides these components, exposure to animal derived material like dander, hair and bristle can be related to increased risk of respiratory diseases. Allergological studies in farming populations in temperate climates have revealed a high prevalence of sensitisation to mites. Inhalation of these substances might result in cellular and immunological responses that could lead to lung diseases. During the last two to three decades there has been a shift in focus concerning respiratory heath in relation to farming exposure from diseases in the parenchyma to diseases in the respiratory tract. Instead of mostly studying allergic alveolitis diseases like "farmers lung", increasing effort has been made to describe chronic bronchitis, bronchial responsiveness and asthma and to look for risk factors therein. Efforts have also been focused on measurements of lung function among farmers and to relate these measurements to values from other groups in the population.

Measurements of exposure (dust, bacteria, moulds, endotoxin and ammonia) and data of sensitisation related to farming occupation are presented. Figures of prevalences, incidences and risk factors to asthma, bronchial responsiveness, chronical bronchitis are described together with data on lung function and risk factors to reduced lung function. The review is restricted to studies in farming populations situated in temperate zones.

EXPOSURE ON FARMS

Dust measurements, total and respirable. The mean values for total and respirable dust exposure measurements with stationary and personal sampling are shown in Tables 1–4.

Summary and remarks. The presented dust exposure data should be compared with care, due to different measurement technique and equipment. The data are based on different sampling times ranging from 30 min [65] in some measurements up to 12 hours [102], and only a few of the data [24, 27] are presented as time weighted average exposure values (TWA). These differences in circumstances under which the sampling took place might be responsible for some of the differences in measured mean values. However, they might also represent a real difference in exposure intensities, and the exposure figures seem to be lowest in cow housings and highest in poultry housings . Some of the listed values for exposure exceed recommended values for continuous exposure of livestock [119] as well as occupational exposure limits for total organic dust in Denmark (3 mg/m^3) [2].

Bacteria and moulds measurements. Up to a third of airborne bacteria in animal housings [8] has been reported to be in the respirable size range (<5µm) and spores for many fungi will also be in the respirable size range. The total number of bacteria is a potential risk factor for respiratory health, and certain bacteria species like gram-negative bacteria might have a greater damaging potential than others [26]. Measurements of bacteria counts are shown in Table 6, and data of mould exposure are shown in Table 7.

Summary and remarks. The presented data of measured colony-forming units of bacteria and moulds should be handled with care, just like the data of dust exposure. Different measurement techniques and equipment have been used in the studies. The differences in exposure might be a reflection of heterogeneity in the condition of the buildings, in the climate, and the time of the year when the sampling took place. There might, however, also be differences in exposure intensities. When comparing the measurement data from the four European countries [96] some of the bias has been avoided due to identical techniques and equipment. The measurements were conducted at the same period of the year and the protocol for the measurements was the same in all countries. The findings from this study [96] indicate a higher exposure to total bacteria in poultry housing compared to pig and cow housing, unlike data concerning exposure to moulds, where no convincing pattern of difference in exposure levels were observed among confinement buildings for different animals. The data from the other referred studies does not contradict this assumption.

Endotoxin measurements, total and respirable. Endotoxins are lipopolysaccharides that are contained in the cell wall of gram-negative bacteria. During the last few years endotoxins have drawn increased attention due to studies [93, 94] suggesting that inhaled endotoxins might play a major part in the etiology of pulmonary inflammation and lung disease, at least from exposure in the grain industry. Therefore, several studies have been conducted to measure the size of the endotxin exposure also in farming. Measurements of total endotoxin are listed in Tables 8–9 and for respirable endotoxin in Tables 10–11.

Summary and remarks. As low as 9 ng/m^3 of pure endotoxin has been reported as inducing adverse pulmonary effect in subjects sensitive to cotton dust [10, 56]. Among healthy subjects in the cotton industry [92] a cross shift decline in FEV_1 has been associated with exposure levels of approximately 100–200 ng/m^3, chest tightness with 300–500 ng/m^3 and fever with 500–1000 ng/m^3. The presented data of exposure to endotoxin in animal housings reflects, therefore, a possible risk for farmers to inhale amounts of endotoxin large enough to induce health effects in the lungs. However, the effect of endotoxin content in cotton dust may be different than the effect of endotoxin in dust from different farming exposures (grain and confinement buildings). Data suggest a higher no effect level in pig feeding exposure than in exposure from cotton dust [30].

Ammonia measurements, stationary and personal. Ammonia originates from urine and faeces. Cows and swine excrete their superfluous nitrogen as urea in the urine and

Table 3. Total dust personal sampling in mg/m^3.

country	housing	N	mean	range	reference
US	swine	55	6.8		24
NL	swine	161	2.6	0.9–5.9	80
US	swine	201	4.53		28
FIN	swine	25	12.6	2.2–40.3	65
NL	swine	360	2.4	0.3–26.6	79
US	swine	151	3.45		86
FIN	cow	5	0.31–3.16		109
FIN	cow	30	5.4	0.5–9.5	65
US	poultry	238	6.5	0.02–81.33	23
FIN	poultry	13	13.0	5.7–37.6	65

1,239 measurements.

The lowest mean value was 0.31 mg/m^3 and the highest was 13.0 mg/m^3 (range 0.02 B 81.33 mg/m^3). There seems to be no differences in exposure levels between stationary and personal samplings. The personal measurements in the animal housings seem to be more even than the stationary ones, although the values measured inside cow houses (mean 0.31 to 5.4 mg/m^3, range 0.5–9.5 mg/m^3) might be lower than those from swine (mean 2.6 to 12.6 mg/m^3, range 0.9–40.3 mg/m^3) -or poultry houses (mean 6.5 to 13.0 mg/m^3 , range of 0.02–81.33 mg/m^3).

Table 4. Respiratory dust personal sampling in mg/m^3.

country	housing	N	mean	range	reference
US	swine	34	0.3		24
D	swine	99	0.3*	0.0–39.4	83
US	swine	201	0.23		28
US	swine	151	0.26		86
US	poultry	210	0.63	0.01–7.73	23

695 measurements. *median.

The lowest mean value was 0.23 mg/m^3 and the highest was 0.63 mg/m^3 (range 0.0–39.4 mg/m^3). The mean values of the personal samplings did not seem to differ from the stationary mean values. Mean values from poultry houses (0.63 mg/m^3, range 0.01–7.73 mg/m^3) houses might be higher than the mean from swine housing (0.23–0.30 mg/m^3, range 0.0–39.4 mg/m^3), although the ranges are quite broad.

Table 5. Gram negative bacteria count in 10^4 CFU†/m^3 stationary sampling.

country	housing	N	mean	range	reference
NL	swine	62	0.77	0.01–0.94	37
CAN	swine	6	0.001–0.02	0–0.46*	15
US	swine	13	0.9		24

81 measurements. *median; †CFU = colony forming units.

The lowest mean value was 0.001 × 10^4 CFU/m^3 and the highest was 0.9 × 10^4 CFU/m^3 (range 0–0.94 × 10^4 CFU/m^3). The exposure assessments from the Netherlands and US are quite similar but exposure data from Canada are much lower.

Table 6. Bacteria count in 10^5 CFU†/m³, stationary sampling.

country	housing	N	mean	range	reference
NL	swine	62	1.073	0.01–36	37
CAN	swine	6	0.81–5.44	0.61–12.5*	15
US	swine	37	14		24
CAN	swine	8	4.25	1.67–9.29	14
EUR#	swine	86	1.28		96
US	cow	181	120	0.15–2600	62
EUR#	cow	86	0.2		96
EUR#	poultry	86	26.9		96

552 measurements. *median; #EUR = UK, NL, DK, D; †CFU = colony forming units.

The lowest mean value was 0.2×10^5 CFU/m³ and the highest was 26.9×10^5 CFU /m³ (range 0.01– 2600×10^5 CFU /m³). The measurements of the mean values do not reveal different exposure levels in the animal housings, but if data from the 4 European countries [96] reflects real differences in exposure, poultry housing (mean 26.9×10^5 CFU /m³) seems to have a higher exposure than pig (mean 1.28×10^5 CFU /m³) and cow housing (mean 0.2×10^5 CFU /m³).

Table 7. Moulds count in 10^3 CFU†/m³, stationary sampling.

country	housing	N	mean	range	reference
CAN	swine	6	0.01–015*	0–0.56	15
US	swine	34	20		24
CAN	swine	8	0.88	0.14–1.81	14
EUR#	swine	68	5.01		96
US	cow	65	19	1.7–1600	62
EUR#	cow	68	6.31		96
EUR#	poultry	68	10		96

317 measurements. *median; #EUR = UK, NL, DK, D; †CFU = colony forming units.

The lowest median value was 0.01 to 0.15×10^3 CFU/m³ and the highest mean value was 20×10^3 CFU/m³ (range 0–1600×10^3 CFU /m³). The exposure does not seem to differ between the animal housings. Viewing the data for the 4 European countries alone [96] gives the same impression of uniform exposure.

Table 8. Total endotoxin in ng/m³, stationary sampling.

country	housing	N	mean	range	reference
CAN	swine	46	1144†	43.8–4131	122
NL	swine	168	130	31–343	37
CAN	swine	8	40.4†	21.5–59.6	14
US	swine	54	200		24
EUR#	swine	110	52.3–186.5		96
EUR#	cow	67	7.4–63.9		96
EUR#	poultry	64	338.9–860.4		96

517 measurements. †Figure in EU/m³, transformed to ng/m³ by dividing by 10; #EUR = UK, NL, DK, D.

The lowest mean value was 7.4 ng/m³ and the highest was 1144 ng/m³. The measurements in Table 8 indicate a higher exposure in poultry houses (mean 338.9–860.4 ng/m³) and swine houses (mean 7.4–1144 ng/m³, range ?–4131 ng/m³) than cow houses (mean 52.3–186.5 ng/m³). Regarding the European data solely [96], exposure in poultry housing seems to be the highest (mean 338.9–860.4 ng/m³), second highest in swine housing (mean 52.3–186.5 ng/m³) and lowest in cow housing (mean 7.4–63.9 ng/m³).

undigested proteins in the faeces. Uric acid (70% of total N) and undigested protein (30% of total N) are the main nitrogen components in the faeces of poultry [75, 118]. Measurements of ammonia in animal housing are shown in Tables 12–13.

Summary and remarks. Of gasses known to be present in animal housings, ammonia is the gas which most frequent by approaches or exceeds the threshold limit values (25 ppm) [2, 24]. Working in animal housings might, therefore, expose farmers to amounts of ammonia severe enough to represent a challenge to the lungs that might induce negative health effects.

SENSITISATION IN FARMERS

Daily occupation as a farmer involves exposure to several allergens in considerable amounts. Most farming populations where allergological studies have taken place, have been situated in temperate climates. Data from France [6], Sweden [34, 36, 60, 61], Denmark [45, 47, 100], UK [5, 17] and Finland [103] have revealed a high prevalence of sensitisation to mites. Except for findings from Finland [103], sensitisation to pollen, animal dander and moulds are less prevalent. In Scandinavia, studies have revealed that sensitisation to *Lepidoglyphus Destructor* seems to be the most prevalent sensitiser of the storage mites, and *Lepidoglyphus Destructor* was the most dominant species in 13 of 16 Swedish barns [35]. Table 14 lists the prevalences of frequent allergens with a positive RAST-test in Scandinavian farming populations. The findings are based on data from [34, 36, 45, 60, 61].

The prevalence data from Hage-Hamsten [34, 36] and Kronqvist [60, 61] are mainly from dairy farming populations, and the study population totalled 440 and 461, respectively. Iversen [45] studied a random sample of farmers with medium sized to large farms in Denmark - 127 pig farmers and 60 dairy farmers. Compared to sensitisation to mites, sensitisation to animal danders, pollen and moulds are less frequent, although sensitisation to timothy grass seems to be high in Kronqvist's data [60, 61]. The prevalence of specific IgE to storage mites was positive in 17% of Scottish stock raising and dairy farmers [17] and between 59% and 9% in Scottish farm-workers [5], depending on respiratory symptoms. High prevalence of positive skin prick test (≥ 3mm) reactions to mites was found among French, mostly dairy farmers [6]. In 664 subjects with no sign of bronchial hyperresponsiveness the prevalence was 15.4% to ≥ one mites (6 in all), 11.6% to ≥ one cereal dusts (6 in all), 5.3%, to ≥ one pollen (5 in all), 5.3% to ≥ on animal danders (6 in all) and 2.6% to ≥ one moulds (3 in all). In 77 subjects with PD_{10} the prevalence was 24.7% to storage mites, 21.3% to cereal dust, 9.1% to pollen, 7.8% to animal dander and 5.2% to moulds. In a cohort of young Danes consisting of 230 female and 1734 male farming students and 407 male rural controls [100] the prevalence of skin prick test (≥ 3mm) was highest for house dust mites, followed by storage mites and timothy in all groups. The skin prick test data from Finland [103] are difficult to compare with results from other studies partly due to the use of other needles than hypodermic and partly due to the presentation in mm^2 rather than in mm or ≥ half the positive control. However, the skin prick reaction to *L. destructor* was the third greatest after cow dander and *Candida albicans*. It is worth considering that for many farmers the occupational exposure to allergens also influences the domestic exposure due to an often close connection between human living quarters and animal housings on farms. Hinze *et al.* [39] found a significant higher concentration of the major cow hair allergen in corridors and bedroom of cow farmers with barn and living quarters in the same building than in farms with separated quarters. Studies from Denmark [47] and Germany [84] have shown large amounts of mites in mattresses of pig farmers. The significance of these finding concerning sensitisation is not clear. Despite a larger content of mites in the mattresses of farmers than of urban dwellers the prevalence of sensitisation was not higher among the farmers than in the general population [84].

During the last three years several studies have been published addressing the relationship between sensitisation and atopic diseases and being raised on a farm, mainly in children [7, 31, 58, 87, 88, 116] but also in adolescents [32, 78] and adults [54, 77]. Farming as the parental occupation was significantly associated with reduced risk for atopic sensitisation (IgE CAP ≥ 2) for outdoors allergens (timothy grass, birth and mugwort) (OR 0.38, 95% CI 0.16–0.87) and for indoors allergens (house dust mite, cat and dog dander) (OR 0.15, 95% CI 0.04–0.57) in 404 Swiss children aged 13–15 years. The risk for atopic sensitisation was lowest in children from full-time farmers (adjusted OR 0.24, 95% CI 0.09-0.66) and less reduced in children from part-time farmers (adjusted OR 0.54, 95% CI 0.15–1.96), indicating a trend in atopic sensitisation from children of non-farming to full-time farming parents [7]. Riedler *et al.* [87] analysed skin prick test data from 1,137 Australian children aged 8–10 years. They found a significant lower prevalence of positive skin prick test reaction to at least one of eight common local allergens in children living on a farm compared to children living outside farms (18.8% *vs.* 32.7%, p = 0.001). Further analysis of the data revealed that regular contact with farm animals was associated with reduced risk of atopic sensitisation (change in OR from 0.48–0.75 after including regular contact with livestock and poultry in the multivariate logistic regression model). In contrast to these findings, the prevalence of positive skin prick test reaction to 15 standardized allergens in a group of 707 7–8 year old children from Gotland in Sweden was the same in children of farmers and non-farmers [58]. However, when analysing for both respiratory symptoms and sensitisation the risk ratio (RR) was lower in children of farmers compared to children of non-farmers (RR 0.28, 95% CI 0.09-0.88). Specific IgE to 7 common aerosolallergens, 6 food allergens and cow epithelium and storage mites was measured in 812 children from Austria, Germany and Switzerland, aged 6–13 years [88]. The risk for sensitisation

Table 9. Total endotoxin in ng/m^3, personal sampling.

country	housing	N	mean	range	reference
US	swine	54	200		24
NL	swine	161	105	41.4–316	80
US	swine	201	20.2†		14
NL	swine	350	92	5.6–1503	79
US	swine	151	17.6		86
US	poultry	236	158.9	0.024–3917	23

1153 measurements.
†Figure in EU/m^3 , transformed to ng/m^3 by dividing by 10.

The level of the mean values measured for total endotoxin from personal sampling is the same as the stationary measurements, lowest mean 20.2 ng/m^3 and highest mean 200 ng/m^3 (range ?-3917 ng/m^3). The mean values reflect no different endotoxin exposure in swine- and poultry housings.

Table 10. Respirable endotoxin in ng/m^3, stationary sampling.

country	housing	N	mean	range	reference
US	swine	3	200		24
EUR#	swine	110	7.4–18.9		96
US	cow	216	1.7	0.016–138	62
EUR#	cow	67	0.6–6.7		96
EUR#	poultry	64	29.6–71.8		96

460 measurements.
#EUR = UK, NL, DK, D.

Lowest mean value was 0.6 ng/m^3 and the highest was 200 ng/m^3. The range was only for one set of measurements [62] and the highest value was lower than the highest mean value measured [24]. The exposure seems to be higher in poultry housing (mean 29.6–71.8 ng/m^3) than in swine- (mean 7.4–18.9 ng/m^3) and cow housing (mean 0.6–6.7 ng/m^3) based on data from the European study [96], although the 3 measurements in US swine housing [24] mean 200 ng/m^3 do not fit into the pattern in the European measurements.

Table 11. Respirable endotoxin in ng/m^3, personal sampling.

country	housing	N	mean	range	reference
D	swine	96	6.7	0.02–444.4	83
US	swine	117	1.7		28
US	swine	151	1.2		86
US	poultry	210	5.9	0.035–69.4	23

574 measurements.

Unlike the broad dispersal in the means from the stationary samplings, the mean endotoxin measurements from personal samplings are quite uniform with the lowest mean of 1.7 ng/m^3 and the highest mean of 6.7 ng/m^3 with no indication of different level of exposure between swine- and poultry housing .The range in measurements was (0.02–444.4 ng/m^3).

Table 12. Ammonia in ppm, stationary sampling.

country	housing	N	mean	range	reference
CAN	swine	54	11.3	2.8–27.3	122
NL	swine	172	5.03	0.23–28.2	37
US	swine	41	9.1		24
US	swine	21	15.9		27
CAN	swine	8	20.8	2.8–38.55	14
UK	swine	56	4.3–12.1	?–58.3	33
NL	swine	56	4.6–18.2	?–59.8	33
DK	swine	56	5.3–14.9	?–43.4	33
D	swine	56	4.5–14.3	?–43.7	33
US	cow	83	6.4	0.1–26.1	62
UK	cow	56	0.3–1.3	?–5.7	33
NL	cow	56	2.9–7.7	?–13.7	33
DK	cow	56	1.9–6.4	?–20.1	33
D	cow	56	1.9–7.1	?–29.3	33
UK	poultry	56	8.3–27.1	?–67.1	33
NL	poultry	56	5.9–29.6	?–72.9	33
DK	poultry	56	6.1–25.2	?–72.3	33
D	poultry	56	1.6–20.8	?–43.3	33

1,051 measurements.

The lowest mean value was 0.3 ppm and the highest was 29.6 ppm (range 0.1–72.9 ppm). There might be a tendency in the measurements that the level of exposure is higher in poultry houses (mean 1.6–29.6 ppm, range ?–72.9 ppm) than exposure in cow houses (mean 0.3–7.7 ppm, range 0.1–29.3 ppm), and possibly also in swine houses (mean 4.3 to 20.8 ppm, range 0.23–59.8 ppm).

Table 13. Ammonia in ppm, personal sampling.

country	housing	N	mean	range	reference
NL	swine	159	1.7	1–6.7	80
D	swine	100	10.9	1.0–60	83
US	swine	201	5.6		28
US	swine	151	5.15		86
US	poultry	174	18.4	0–75	23

785 measurements.

The lowest mean value was 1.7 ppm and the highest was 18.4 ppm. The range was (0–75 ppm). The level of exposure seems to be the same from stationary and personal samplings measurements. Like values from stationary measurements, the exposure in poultry houses mean 18.4 ppm (range 0–75 ppm) seems to be higher than in swine houses mean 1.7–10.9 (range 1–60) when measuring personal samplings. No data are available for exposure in cow houses.

was less for children living on farms compared to children living outside farms (OR 0.61, 95% CI 0.41–0.92) and the difference was greatest for sensitisation to grass pollen. Atopic sensitisation was lowest in children exposed to stables and consumption of cow milk in their first year compared to those exposed from their first to their fifth year (12% *vs.* 29%), and the lowest prevalence of sensitisation was found among children exposed to stables up to 5 years of age. Studies in children outside Europe [31] have found similar results. The risk for a positive skin prick test reaction in Australian children aged 7–12 years was lower for children living on a farm for at least one year compared to children with no residential time on a farm (adjusted OR 0.47, 95% CI 0.32–0.72), from one of two rural towns included. Livestock farms were argued to reduce the risk for sensitisation. Data from a questionnaire survey of 10,163 Bavarian children aged 5–7 years [116] seems to support the argument for an association between livestock farms and sensitisation. Among farmers' children, increasing exposure to livestock was related to a decreasing prevalence of atopic diseases (adjusted OR 0.41, 95% CI 0.23–0.74). As in smaller children, the same pattern of difference in sensitisation has been found in adolescents described in a study from Canada of 1,199 secondary school students aged 12–19 years [32]. Children raised on farms were less at risk of being sensitised to any one of 24 common inhalant allergens measured by prick test reaction, than children raised outside farms (adjusted OR 0.57, 96% CI 0.46–0.75). Data from a study of 1,501 Danish farming students and rural controls aged 19–20 years show the same tendency [78]. The risk of a positive prick test reaction to at least one of five inhalant allergens (house dust mite, timothy, birch, cat and dog) were lower among subjects raised on farms compared to subjects raised outside farms (OR 0.62, 95% CI 0.39–0.98). Specific IgE measurements of the same allergens showed the same pattern, although this was non-significant. Slightly older subjects were studied by Kilpeläinen *et al.* [54]. In their study in a group of 10,667 Finnish university students aged 18–24 years, subjects raised on farms had a reduced risk of a physician diagnosing allergic rhinitis and/or allergic conjunctivitis (adjusted OR 0.63, 95% CI 0.50–0.79, p = 0.001) and for diagnosing asthma and episodic wheezing (adjusted OR 0.71, 95% CI 0.54–0.93, p = 0.05). A similar protective effect of being raised on a farm was found in a prospective birth group study of 5,192 Finnish subjects followed up to the age of 31 years [77]. High parity and being a farmer's child was associated with decreased risk of atopy (skin prick test to three of the most common allergens in Finland and to house dust mite) (adjusted OR 0.50, 95% CI 0.42–0.60).

The reason for this possible protective effect of being raised on a farm to sensitisation is not clear, but exposure to immune modulating materials like bacteria or components of the bacteria wall, e.g. endotoxin, in early life has been suggested as structures of importance. Bacteria, both gram-positive and negative, together with endotoxin, have been measured in high concentrations in stables and confinement buildings [14, 15, 24, 37, 62, 96, 117, 120, 122] and contact to livestock and poultry have been reported in several studies [87, 88, 31, 116] as an essential factor to the reduced risk of atopic sensitisation among subjects raised on farms. The drinking of non-pasteurised cow milk from farms represents an endotoxin and bacteria exposure to the gastrointestinal tract [88] that might offer a similar protective effect towards sensitisation as exposure to animal housings. This challenge of bacteria and bacteria components to the lungs and gastrointestinal tract can activate antigen-presenting cells and give rise to a high T-helper-1-cell immune activity by production of tumour necrosis factor, interferon gamma, interleukin 12, and interleukin 18. [88] With a high T-helper-1-cell immune activity to allergen challenge the activation of immunoglobulin E is less likely to appear, thus reducing the risk of atopic sensitisation and diseases.

Summary and remarks. Mites seem to be the most prevalent allergen leading to sensitisation in farming populations in Scandinavia, and among the storage mites sensitisation towards *Lepidoglyphus Destructor* are the most prevalent [34, 35, 36, 45, 60, 61, 100]. There are signs indicating that working exposure in farming also influences the domestic area [39, 47, 84] and there might be a protective effect in being raised on a farm regarding sensitisation to common inhalant allergens [7, 31, 32, 54, 58, 77, 78, 84, 87, 88, 116]. Challenges to bacteria and bacteria structures due to exposure to animal housings [31, 87, 88, 116] and consumption of raw cow milk might be important protective factors [88].

RESPIRATORY SYMPTOMS IN FARMERS

Cross-sectional studies of chronic bronchitis. Data from 9,017 farmers [105] revealed a significant effect of atopy and smoking on the prevalence of chronic bronchitis. There was an increase in rate/1,000 (standardised for sex and age) of the disease from 41 in non-atopic non-smokers through 101 in atopic non-smokers, and 106 in non-atopic smokers to 257 in atopic smokers. Later studies from a larger group of Finnish farmers consisting of 18,351 subjects [104] found that chronic bronchitis was associated with atopy (RR 1.43) and smoking (RR 2.43). In a Norwegian study of 10,792 farmers [70] the prevalence of chronic bronchitis was highest among full-time farmers with livestock production 11.2% (OR 2.48, 95% CI 1.59–3.88) and lowest among part-time farmers with no livestock production 4.4%. Smoking did significantly influence the prevalence of chronic bronchitis - 5.8% in never smokers and 13.5% in ever smokers (OR 2.53, 95% CI 2.13–2.99). Full-time farmers with livestock production (8.4%) had a higher prevalence of chronic bronchitis than farmers with no livestock production (5.9%) (OR 1.99, 95% CI 1.31–3.01). The highest prevalence of chronic bronchitis was among farmers with poultry livestock (13.2%) (OR 5.05, 95% CI 2.33–11.0) and among farmers with both cows and horses (13.9%) (OR 5.41, 95% CI 2.29–12.8). Iversen *et al*. [49] found in their study of a representative sample of 1,685

Table 14. Prevalences of sensitisation in Scandinavian farming populations to frequent environmental and occupation allergens (RAST-tests).

Allergen	Hage-Hamsten 1985-87	Iversen 1990	Kronqvist 1999
Mites			
L. destructor	6.8	3.2	6.6
T. putrescentia	4.4	1.6	6.2
A. siro	3.9	1.1	6.2
D. pteronyssinus	6.0	5.9	7.3
Animal danders			
Dog	0.9	0	3.4
Cow	3.8	1.1	5.7
Swine	n.d	1.1	n.d
Pollens			
Birch	1.9	0.5	3.9
Timothy	4.9	1.1	8.1
Moulds			
C. herbarum	0.9	0	3.4

n.d. = not determined.

Danish farmers that the prevalence of chronic bronchitis was 23.6%; in farmers aged 31–50 years - 17.9% and in farmers aged 51–70 years - 33.0%. The prevalence was highest among pig farmers (32.0%) and farmers with both dairy production and pig farming (28.4%) and lowest among dairy farmers (17.5%) and farmers with no livestock (18.6%). Pig farming (OR 1.53) was a risk factor for chronic bronchitis in a logistic regression analysis with correction for age and smoking. Like the Danish data, the prevalence of chronic bronchitis from Canada [121] was highest among swine producers when analysing the distribution of the disease between 249 swine producers (15.3%), 251 grain producers (7.2%) and 263 non-farming subjects (5.7%). The respiratory symptoms were associated with the daily number of working hours.

Prevalence studies of chronic bronchitis in swine farming and non-exposed control settings [16, 113] from Canada and the Netherlands have found increased prevalence among subjects exposed to swine confinement buildings. Cormier *et al.* [16] found a significant higher prevalence of 17.5% in exposed subjects compared to 11.6% among controls. Exposed subjects working more than 3 hours in swine confinement buildings had a higher prevalence of chronic bronchitis than those working less hours. Data from the Netherlands [113] based on analysis of 239 pig farmers and 311 rural controls revealed a significant higher prevalence of chronic bronchitis in pig farmers (20.2%) than controls (7.7%). Atopy in childhood was not associated with the prevalence of chronic bronchitis. Danuser *et al.* [22] found in their study of 904 randomly selected Swiss farmers a prevalence of chronic bronchitis of 16%, significantly increasing with age. Risk factors to chronic bronchitis were crop farming (OR 2.32, 95% CI 1.03–5.23), age >60 years (OR 2.40, 95% CI 1.43–4.00), former smoker (OR 1.60, 95% CI 1.03-2.48) and >4 hours in confinement buildings a day (OR 2.61, 95% CI 1.01–6.76). In non-smokers the prevalence of chronic bronchitis was significantly more prevalent among Swiss farmers (12.0%) than among the Swiss population (SAPALDIA) (6.8%) (adjusted OR 1.89, 95% CI 1.32-2.95). A slightly lower prevalence of chronic bronchitis (9.4%) was described in a study from New Zealand of 1,706 randomly selected farmers [55]. The highest prevalence (21.1%) among farmers raising horses was quite interesting. Significant risk factors to chronic bronchitis were eczema or rhinitis (OR 1.6, 95% CI 1.1–2.2), smoking (OR 2.2, 95% CI 1.2–2.5), hay handling (OR 1.6, 95% CI 1.1–2.3) and horses (OR 1.6, 95% CI 1.1–2.5). In a study of a random sample of 7,496 European farmers from Denmark, Northern Germany, Switzerland and Spain, [82] no data of chronic bronchitis was presented, but the prevalence of chronic phlegm was significantly higher in farmers aged 20–44 years (9.4, 95%CI 8.3-10.5) compared to an aged matched sample of the general European population (ECRHS) (7.5, 95% CI 6.5–8.5). Among pig and poultry farmers there was a significant dose-response relationship between cough with phlegm and hours inside animal housings.

Several studies from France have focused on exposure from dairy farming and respiratory health. Dalphin *et al*. [20] found a significant higher prevalence of chronic bronchitis among 250 dairy farmers (12%) compared to 250 control subjects (6%). Especially among subjects aged 40 years or more and in non-smokers the disease was frequent. In a study from the same group published in 1998 [18] the prevalence of chronic bronchitis was 6.4% among 265 dairy farmers compared to 0.7% among 149 non-exposed controls (OR 11.8, 95% CI 1.4–97.1). There was a non-significant increase in the prevalence of chronic bronchitis in smokers, both exposed and controls, and the effect of exposure was higher than or equal to the effect of smoking on chronic bronchitis. Logistic regression showed a synergistic effect of exposure and smoking on chronic cough. In a study of risk factors for chronic bronchitis among 5,703 French dairy farmers [21] the prevalence was 9.3% and significant risk factors for chronic bronchitis were male sex, age, smoking and altitude. The prevalence of chronic bronchitis was 12–14% in farmers living in districts located between 700–1,000 meters altitude. The prevalence of chronic bronchitis was studied in 236 livestock farm-workers (169 male and 67 female) from Croatian farms raising dairy cattle and horses, and in 165 (125 male and 40 female) food packing workers.[73]. Chronic bronchitis was significantly more prevalent among male farm-workers (21.9%) than among controls (6.7%), ($p < 0.05$) and smokers had a higher prevalence of chronic bronchitis (27.6%) than non-smokers (6.5%), ($p < 0.05$). No differences were observed in females, neither between farm-workers and controls nor between smokers and non-smokers.

The effect of smoking and grain exposure was studied in a Canadian survey [11] comprising 1,633 subjects. In males the prevalence of chronic bronchitis was the same between those exposed and non-exposed to grain dust, both for smokers and non-smokers. Among non-smoking females the prevalence was as in males equal in grain dust exposed (2.0%) and non-exposed (2.1%), but in female smokers a significant difference in the prevalence was found between grain exposed (13.2%) and non-exposed (5.9%) (OR 3.55, 95% CI 1.06-11.30), suggesting an interactive effect of grain dust exposure and smoking on chronic bronchitis in women. Contradictory to the findings of Chen *et al.* [11] no effect of grain dust exposure from farming on respiratory health was observed in another Canadian survey [67] involving 924 males and 968 females from a rural community. This study found a significant effect of smoking on respiratory symptoms, but no interactive effect of grain and smoking exposure, neither for males nor females. Kern *et al.* [53] studied the prevalence of chronic bronchitis in 814 farm-workers (738 male and 76 female) from farms with no breeding or managing livestock and in 570 male and 65 female food packing workers. Chronic bronchitis was significantly more prevalent among male farm-workers (20.9%) than among controls (7.4%), ($p < 0.001$) and smokers had a higher prevalence of chronic bronchitis (30.2%) than non-smokers (6.9%), ($p < 0.001$), No differences were observed in females, neither between farm-workers and controls nor between smokers and non-smokers.

One of the very few studies to address other farming exposures than swine-, dairy- or grain exposures in relation to respiratory symptoms was published by Zuskin *et al.* [125]. In their study of 135 female and 32 male greenhouse workers and 51 female and 30 male non-exposed office workers as controls they found a non-significant increase in chronic bronchitis in both female and male greenhouse workers compared to female and male controls.

Apart from a Danish study [100], most studies in farming populations concerning chronic bronchitis have focused on farmers who have been in the trade for years. Sigsgaard *et al.* [100] found among 1,901 farming students, of whom 210 were females and 407 rural control aged 19 years, a prevalence of chronic bronchitis between 0-4.8%. There was no gender difference, and smoking only significantly increased the prevalence in the male farming students (1.1% *vs.* 3.0%).

Longitudinal studies of chronic bronchitis. Incidence data of chronic bronchitis in farming settings are almost exclusively based upon studies from Finland. Terho *et al.* [105] followed 6,899 farmers with no chronic bronchitis in the beginning for 3 years. Standardised incidence rates of chronic bronchitis (per 1,000 farm years) were 14 among non-smoking non-atopic subjects, 34 among atopic non-smoking subjects, 36 among non-atopic smoking subjects and 50 among atopic smoking subjects ($p < 0.001$). The relative risk of chronic bronchitis from incidence data adjusted for age, sex, smoking, or atopy, by logistic regression was 2.2 for atopy (95% CI 1.8–2.7) and 2.3 for smoking (95% CI 1.8-2.9). In an extension of the analysis in a larger population of 17,134 subjects comprising of data from postal surveys in 1975 and 1981 from the Finnish twin group Terho *et al*. [104] found that chronic bronchitis was related to atopy (RR 1.28), smoking (RR 2.31) and farming (RR 1.45). The authors concluded that the data supported the "Dutch hypothesis" on the aetiology of chronic bronchitis. A study also based upon data from the Finnish twin Registry focused on the role of the environment in the development of chronic bronchitis. Husman *et al.* [42] found the same prevalence of chronic bronchitis among non-smoking farmers (3.6%) as among corresponding non-farming group (3.4%). However, the 6 years incidence of chronic bronchitis was 2.7% and 0.7%, respectively, ($p < 0.001$) indicating that chronic bronchitis is a work-related disease among farmers. Analysing for jobs in farming associated to the development of chronic bronchitis, Voholen *et al.* [115] conducted a study comprising of 12,056 farmers. The incidence of chronic bronchitis was 2,687 new cases annually per 100,000 farmers. Chronic bronchitis was most common among farmers with livestock production compared to farmers with grain production. In livestock production, chronic bronchitis was strongly associated with tending swine. Analysing for 147 characteristics of the farming occupation, the methods of grain handling and drying were the most important factors for predisposing farmers to chronic bronchitis.

Summary and remarks. The range in prevalence of chronic bronchitis in the farming population is wide, from 2% in female Canadian non-smoking grain farmers [11] to 32% in Danish pig farmers [70]. Compared to the range in prevalence in the non-farming control groups from 0.7% in French controls (18) to 11.6% in Canadian controls, the prevalence of chronic bronchitis seems to be increased, also when compared with prevalence data from general population studies from Scandinavia 3.0–4.6% [63, 72].

Longitudinal studies of chronic bronchitis in farming populations suggest that the disease is work-related in farmers [42].

From both cross sectional- and longitudinal studies, atopy [104, 105], smoking [21, 55, 104, 105], and swine farming [49, 115] have been found as risk factors associated with chronic bronchitis. Cross-sectional studies alone have related eczema or rhinitis [55], former smoking [22], livestock production [70], horses [55], > 4 hours in confinement buildings [22], crop handling [22], hay handling [55] male gender [21], age [21, 22] and altitude of farming [21] as risk factors and in a longitudinal study [104] work as a farmer was a risk factor.

Cross sectional studies of asthma. The mean prevalence of asthma in a representative sample of 1,685 Danish farmers [49] was 7.7%, lowest (3.6%) among farmers aged 30–49 and highest (11.8%) among farmers aged 50–69 years. The prevalence of asthma was highest among pig farmers (10.9%) although there was no significant difference in the prevalence to farmers with no animal production (7.5%), farmers with both swine- and dairy production (6.4%) and dairy farmers (5.5%). Logistic regression analysis revealed that age (OR 5.8, 95% CI 2.8–12.2) and pig farming (OR 2.0, 95% CI 2.0–3.5) were risk factors for self-reported asthma. The prevalence of asthma among farmers and aged matched subjects from a representative sample of the Danish populations was the same in the age group 30–49 years, but significantly higher among farmers aged 50–69 compared with aged matched subjects from the same sample (OR 2.25, $p < 0.001$). The life time prevalence of asthma in Norwegian farmers [69] was 6.3% and in the same range as data from the Danish study [49]. The prevalence for current asthma (now) was 3.1%. In the Norwegian study consisting of a population of 8,482 farmers and their spouses [69], significant risk factors to current asthma were asthma among parents or siblings (OR 2.9, 95% CI 2.1–3.9), asthma as a child or adolescent (OR 22.2, 95% CI 15.2–32.4), animal production (OR 1.6, 95% CI 1.1–2.2) and age from 40–69 years (OR 1.8 to 4.6, 95% CI 1.1–7.5).

The risk of having current asthma in non-smokers increased from OR 1 in subjects with no asthma in the family and no animals, to OR 1.9 (95% CI 0.4–8.9) in subjects with asthma in the family and no animals, to OR 2.2 (95% CI 1.1–4.2) in subjects with no asthma in the family and animal production, to OR 6.3 (95% CI 3.1–13.1) in subjects with animal production and asthma in the family. A combination of animal production, smoking and a positive family history of asthma gave an OR of 8.1 (95% CI 4.0–16.2). The authors concluded that the data supports a hypothesis of an interaction between gene and environment factors. Figures of the prevalence of asthma in 1,706 farmers from New Zealand of current asthma expressed as 12 month overall period prevalence was much higher (11.8%) than that observed in Scandinavia (2.1%) [56]. Despite this considerably higher prevalence in the farmers from New Zealand, the prevalence was less than the prevalence of asthma measured in the general population (15%). Only for farmers occupied with horse breeding/ grooming (16.5%), pig farming (18.2%), poultry farming (17.4%) and in harvesting oats (17.4%) was the prevalence higher than in the general population, but not significantly so. Data from the study suggested a gender difference in the prevalence of asthma with increased risk for female farmers, (OR 1.8, 95% CI 1.3–2.5). Significant increased risk of asthma-like symptoms was also found for females (OR (males) 0.5, 95% CI 0.3–0.8) in a Danish study of 1,901 farming students of whom 210 were females and in 407 rural controls [74]. Asthma in the family (OR 1.6–3.4) and smoking (OR 1.7, 95% CI 1.2–2.4) were also factors significantly associated to asthma. The prevalence of asthma-like symptoms was between 5.4–21%, but no difference was observed between farming students and controls. High prevalence of asthma (18.3%) was also found among 904 randomly selected Swiss farmers [22], but no difference was observed in the prevalence of asthma attacks between farmers (2.1%) and a random sample of the Swiss population (3.1%). Current (OR 2.14, 95% CI 1.43–3.19) and former smoking (OR 2.05, 95% CI 1.34–3.14) were risk factors to asthma. Exposures other than the production of animals and grain have been reported as associated with increased risk of asthma in farming populations. Senthilselvan *et al.* [99] found in their study of 1,939 male farmers an increased risk of asthma in subjects exposed to carbamate insecticides (OR 1.8, 95% CI 1.1–3.1). Occupational asthma was assessed in a European Community study consisting of pooled data from 10 European countries besides New Zealand and USA from a total of 26 selected areas [59]. In the study population comprising 15,636 subjects aged 20–44 years, the highest risk of asthma - defined as bronchial hyperresponsiveness to methacholine - and reported asthma symptoms or asthma medication was shown in farmers (OR 2.62, 95% CI 1.29–5.35). The result for farmers, together with the result for painters, were the most consistent throughout the countries. There was an increasing risk of asthma with increasing exposure for organic dust at work - none (OR 1), low (OR 1.15, 95% CI 0.92–1.44) and high (OR 1.40, 95% CI 1.01–1.93). The same trend was observed for inorganic dust and gases and fumes. The data was based on a job-exposure matrix. The proportion of asthma among young adults attributed to occupation was 5–10%, implying that, given a mean prevalence of asthma of about 5%, occupation is the cause of 0.2–0.5% of prevalent cases of asthma or the cause of exacerbation of their asthma. In contrast to these findings, the prevalence of asthma (2.8%, 95% CI 2.4–3.2) in a random sample of 7,496 European farmers from Denmark, Northern Germany, Switzerland and Spain [82] was lower, and when comparing the prevalence of asthma among the farmers aged 20–44 (1.3% , 95% CI 0.9–1.7) with the prevalence in an aged matched sample of the general European population (ECRHS) (3.2%, 95% CI 2.9–3.9), the difference was significant (p = 0.001). Data of the prevalence of occupational asthma from two studies in farm-workers [53, 73] from Croatia did not support the findings from the European Community study. No differences in the prevalence of occupational asthma (0–7.7%) were observed among the 236 livestock - [73] and among the 814 crop farm-workers [53] and food packing controls, for neither smokers nor non-smokers.

The asthma prevalence has been measured in pig farmers and analysed in relation to asthma among a non-exposed control group. Vogelzang *et al.* [113] found in a study of 239 pig farmers and 311 rural controls the same prevalence of asthma in the two groups (5.9%) *vs.* (5.5%). In pig farmers the use of disinfectants (quaternary ammonium compounds) (OR 9.4, 95% CI 1.6–57.2) and aspects of disinfecting procedure were associated with the prevalence of asthma. Atopy was significantly less prevalent in pig farmers (4.6%) compared to controls (14.6%) and pig farmers had significantly less symptoms of allergy in childhood (9.9%) than controls (17.2%). Atopy in childhood was strongly associated with the prevalence of asthma symptoms (OR 4.1, 95% CI 2.2–7.7). In another study in 194 pig farmers from the Netherlands [84], risk factors for asthma were analysed. Preller *et al.* found that atopic sensitisation to common allergens was associated with the use of quaternary ammonium compounds disinfectants (OR 7.4, 95% CI 1.3–43.1). Disinfectants were further associated with symptoms consistent with asthma, but only in subjects with atopy (OR 4.4, 95% CI 1.3–14.6). Among pig farmers with atopy and a fall in FEV_1 of 10% after histamine challenge (PC10) the OR was 8.2 (95% CI 1.6–42.6). In pig farmers with atopy and a positive PC10, and exposed to endotoxin > 101 ng/m^3, the risk of symptoms consistent with asthma was increased (OR 6.1, 95% CI 1.0–36.2).

In a mainly dairy (74%) dominated farming population in Sweden [85] the prevalence of asthma among the 6,702 participating subjects was 2.1%. Most of them, 4,373, were full time farmers (65%) of whom 80% were men. The mean age was 45.6 (12.5) years for men and 45.1 (12.3) years for women. Most were non-smokers, 57% of the men (72% of the women); 21% of the men (11% of the women) were ex-smokers and 21% of the men (18% of the women) were current smokers. A substantial higher number of prevalent cases of asthma (15%) were found among 162 Scottish dairy and 128 cattle-beef farmers [17]. French data [18] of asthma prevalence among dairy farmers and controls are much lower than figures from Scotland [17], and in the same range as the data from Sweden [66]. The cross-sectional data from analysis of 265 dairy farmers and 149 non-exposed controls revealed the same cumulative prevalence of self-reported asthma and of current asthma in farmers and in controls; 5.3% and 1.5%, respectively, *vs.* 3.4% and 1.3%. In two [60, 61] studies from the island of Gotland in Sweden, change in prevalence over time and risk factors to asthma have been analysed. 461 dairy farmers were investigated in 1995 and 65 (14.1%) of these subjects participated in the study in 1984. The prevalence of asthma increased significantly from 5.3–9.8%, but the prevalence of storage mite allergy was the same in about 6%. Significant risk factors for asthma were sensitisation to: mites (OR 3.5, 95% CI 2.1–5.8), to pollens (OR 4.9, 95% CI 2.9–8.3), animal danders (OR 4.1, 95% CI 2.4–7.0), insects (OR 2.7, 95% CI 2.4–7.0), moulds (OR 2.5, 95% CI 1.2–5.2) and FEV_1 < 80% (OR 3.2, 95% CI 1.8–5.6).

Prevalence data of asthma in non-animal farming occupation has been analysed among grain farmers [97] and for exposure in greenhouses [125]. In a Canadian study [97] comprising 1,634 subjects the prevalence of asthma was 3.8%. Significant predictors for asthma were grain farming (OR 1.9, 95% CI 1.3-2.5), sex (male) (OR 1.9, 95% CI 1.1-3.2). Stratified for sex, grain farming was a significant predictor for asthma, but only in men. In a cross-sectional study of 135 female and 32 male greenhouse workers [125] no significant increase in the prevalence of asthma was observed compared to non-exposed 51 female and 30 male controls, neither for males (6.3% *vs.* 0%) nor for females (0.7% *vs.* 0%). Recent published data from a pooled analysis of 4,793 crop farmers from four European countries [71] found a prevalence of asthma of 3.3%. Flower growing was a significant risk factor (OR 2.1, 95% CI 1.1–3.9) and working inside the greenhouses was a marginal risk factor (OR 2.1, 95% CI 0.9–4.5) for asthma using a multivariate model adjusted for age, sex, smoking, country, and other plants or livestocks.

Longitudinal studies of asthma. No longitudinal studies on incidence of asthma in farming populations have been published, and figures of asthma incidence associated with farming are based on data from surveillance systems for occupational diseases, including asthma. These systems are mainly made for insurance and compensation purposes for the work force [52]. The data sources are different, there are differences in the definition of occupational asthma between the countries and heterogeneity in classification of occupation. Some surveillance programme do not have information about whether farming is classified as an occupation. Due to weakness in coverage and case ascertainment, from these figures there might, therefore, be a general tendency in under-reporting of asthma in farming and other jobs. From those surveillance systems where data from farming occupation are present, the incidence figures from Finland [52] are by far the highest. The mean annual incidence rate of 174 cases / 10^6 employed workers, and the mean annual incidence rate for male farmers was 1,200, and for female farmers 1,910. These high figures in the farming population are probably due to the custom in the Finnish farming population to brush their cows daily. Data from Germany [3] have a compensatory scheme as the source of data. The annual mean incidence rate was 51/ 10^6 employed workers, while in farmers the figure was 113. Swedish surveillance data [106] are based on self-reported asthma, and here the mean annual incidence rate was 80 cases /10^6 employed workers, in male farmers 179 and in female farmers 203. By far the lowest data on incidence of occupational asthma has been reported from the state of Michigan in the USA, [90]. These data originate from physician's reports, compensation claims and hospitals. The annual mean incidence rate was 30/10^6 employed workers, while in agricultural production the figure was only 3.

Summary and remarks. The range in prevalence of self-reported asthma has been found to range from 0.7% in female greenhouse workers [125] to 21% in Danish female farming students who smoked [74]. Compared to the range in prevalence in the non-farming control groups from 0% in female controls to greenhouse workers [125] to 13.2% in Danish controls [74], and with the range in prevalence data (2.9-7.2%) from general populations from Scandinavia [40, 76, 107] self-reported asthma in farming population seems to be higher among farmers. However, apart from the prevalence data from the UK [17]; based on 290 farmers (15%), the Danish data [74] based on 62 smoking females (21%), the data from Switzerland (18.3%) based on 904 farmers, and the data of current asthma from New Zealand [56], the prevalence figures are between 0.7–7.7% in farming populations, which is close to prevalence data from the general population in Scandinavia. In one study of European farmers [82] the prevalence figure was lower among the farmers than in the general population. These findings, together with data of no difference in the prevalence of asthma between farmers and controls in Danish [74] and the Swiss [82] studies, indicate that there might not be an increased prevalence of self-reported asthma in the farming industry.

The probable uniformity in prevalence might be due to little or no effect of farming. However, healthy worker selection, heterogeneity in diagnosis, misclassification, age differences, difference in time of study and small study populations resulting in low statistical power, might also be factors explaining why no difference is observed. There is a need for well-designed longitudinal studies of incidence of asthma and risk factors to clarify whether asthma should be regarded as an occupational lung disease in farming.

Several risk factors for self-reported asthma have been published in cross-sectional studies. Age [49, 69], asthma in the family [69, 74] and asthma or atopy as a child [69, 113] and gender - both female and male [56, 74, 97], together with low FEV_1 [60], have been found as risk factors. Environmental factors such as smoking [22, 74], animal production [69], pig farming [49], grain farming [97], flower growing [71], organic dust at work [59], carbamate insecticides [99], disinfectant [113], as well as sensitisation to mites, pollen, animal dander, insects and moulds [60], are also significant risk factors for self-reported asthma.

Cross-sectional studies of bronchial responsiveness. Studies of bronchial responsiveness to histamine or methacholine challenge have been performed in farming populations, although the studies are few and most of them are small in the number of enrolled subjects. In a study from Western France [13] involving 102 pig farmes, 51 dairy farmers and 51 non-farming referents, the participants were challenged with methacholine up to a dose of 500 mg. Only four subjects had a fall in $FEV_1 > 20\%$. The prevalence of PD_{10} (fall in $FEV_1 > 10\%$ up to the dose given) was 35.6 among dairy farmers, 17.9% among pig farmers and significantly lower 6.7% among controls. Data for PD_{15} showed the same trend. A similar finding, although non-significant, was found in a study by Rylander *et al*. [91]. The bronchial methacholine response was a 10.2% decrease in FEV_1 in dairy farmers (n = 23), a 9.2% decrease in FEV_1 in swine farmers (n = 36), and a 4.9% decrease in FEV_1 in controls (n = 16). Carvalheiro *et al*. [9] studied the response to methacholine (up to 1.25 mg) as the decrease in FEV_1 (ml) from baseline to the highest dose of methacholine given to 20 grain/vegetable farmers, 20 dairy/poultry farmers, 36 swine farmers and 23 non-exposed controls. The decrease in FEV_1 was significantly higher among farmers with animal production (300 ml) compared to agricultural farmers and controls (100 ml). A study from Denmark [44] analysed the bronchial hyperresponsiveness to histamine in three subsamples from a population of 1,175 male farmers; 47 subjects with asthma (group I), 63 subjects with respiratory symptoms like wheezing, shortness of breath or cough without phlegm (group II), and 34 subjects with no respiratory symptoms (group III). The prevalence of bronchial hyperreactivity ($PC_{20} \leq 8$ mg/ml) was very high in all groups, (95% in group I, 66% in group II and 59% in group III). Bronchial hyperreactivity was significantly associated with age and standardised residual of FEV_1 in farmers from group II. From the same group [48], bronchial responsiveness to histamine was measured among 124 pig farmers and 57 dairy farmers. Data revealed a non-significant difference in mean PC_{20} between pig farmers (11.7 mg/ml) and dairy farmers (16.8 mg/ml), as well as in the prevalence of positive PC_{20} subjects; pig farmers (50%) and dairy farmers (42%). In another study from Denmark, Sigsgaard *et al.* [100] found among 1,901 farming students of whom 210 were females, and among 407 rural male controls ages 19 years, a prevalence of unspecific bronchial hyperresponsiveness between 7.2–12.4%, lowest in male smoking rural controls and highest in male smoking farming students. There was no gender difference, and smoking only significantly increased the prevalence in the male farming students (8.1% *vs.* 12.4%). A thorough Swedish study [64] of 20 respiratory healthy pig swine confinements workers and 20 respiratory healthy non-rural controls analysed for alteration in bronchioalveolar lavage, lung function and bronchial reactivity. No differences in bronchial responsiveness to methacholine was observed between the groups; however, there was a significant elevation in total cell count and in the concentration in neutrophils granulocytes in swine confinement workers compared to controls. The number was the same regarding concentration of alveolar macrophages, eosinophils and lymphocytes. Data from the study indicated that randomly reselected pig farmers had signs of airway inflammatory reaction and activation of the immune system without alteration in lung function or bronchial reactivity. As opposed to the Swedish study, a Canadian study [123] comprising 20 swine farmers and 20 controls randomly selected from outdoor city workers, found a significant increased bronchial responsiveness to methacholine (up to 256 mg/ml) among swine farmers compared to controls. The mean concentration for PC_{10} (77.2 mg/ml *vs.* 180.8 mg/ml) and PC_{20} (154.5 mg/ml *vs.* 229.6 mg/ml) was significantly lower in swine farmers than controls, and the number of subjects with a positive PC_{20} were significantly higher among swine farmers than controls. Besette *et al.* [4] studied bronchial responsiveness to methacholine up to a dose of 256 mg/ml in 60 pig farmers. Group 1 (n = 16) consisted of asymptomatic subjects with normal spirometry. In group 2 (n = 17), all were asymptomatic with $FEV_1/FVC < 95\%$ (n = 14) predicted, and in group 3 (n = 13) subjects had chronic bronchitis with normal lung function. Subjects in group 4 (n = 14) were symptomatic with $FEV_1/FVC < 95\%$. Subjects from group 4 had a significantly lower PC_{20} value compared to the other groups, and the number of subjects with $PC_{20} < 16$ mg/ml were larger in this group. Bronchial responsiveness has also been assessed in small scale studies in dairy farming. Amishima *et al.* [1] found an increased responsiveness to methacholine among 37 dairy farmers compared to 11 healthy nonfarming controls. The cumulative concentration inducing a 35% fall in respiratory conductance ($PD_{35}Grs$) was used to measure bronchial hyperresponsiveness. No differences were observed in the bronchial response among the three different subgroups of dairy farmers (12 farmers with episodes of farmers lung, 13 farmers with serum antibody to Micropolyspora faeni and/or Thermoactinomycetes vulgaris but no symptoms, and 12 dairy farmers with no serum antibodies and no symptoms). Analyses of risk factors to bronchial responsiveness have been studied by Vogenzang *et al.* [114]. In a study of 96 pig farmers with chronic respiratory symptoms, and among 100 pig farmers with no respiratory symptoms, they found that mild bronchial hyperresponsiveness ($PC_{10} \leq 16$ mg/ml) was associated with the use of quaternary ammonium compounds (OR 6.7, 95% CI 1.4–32.8), wood shavings as bedding (OR 13.3, 95% CI 1.3–136.7), automated dry feeding material (OR 4.8, 95% CI 1.0–7.8), pellets as feeding material (OR 4.8, 95% CI 1.1–21.1) and location of air exhaust via pit or roof in the confinement units (OR 2.7, 95% CI 1.2–6.3). No association between bronchial responsiveness and exposure to dust, endotoxin or ammonia was observed. In a Danish study [101] in the same group as described in [100], analyses were undertaken to assess the influence of genetic and environmental factors on respiratory health. Pi-alleles to α_1-antitrypsin were found to be associated to bronchial hyperresponsiveness, but only among farming students, suggesting a gene environmental interaction. The odds ratio (OR) for bronchial hyperresponsiveness increased in subjects with increasing rareness of the Pi-alleles. The OR for MS was 1.71 (95% CI 0.84–3.49), for MZ the OR 1.93 (95% CI 1.06–33.39) and for rare Pi alleles (SZ, SS ZZ) the OR was 4.39 (95% CI 1.19–15.8). Bohadana *et al.* [6] analysed for risk factors to bronchial responsiveness in 741 French farmers, mainly dairy farmers. Reactors were those that fell in $FEV_1 \geq 10\%$ after a single dose of acetylcholine (1,200 mg) and those subjects with a prechallenge $FEV_1 < 80\%$ that increased in FEV_1 by > 10% and exceeded 200 ml after inhalation of 300 mg salbutamol. 77 subjects (10.3) were reactors. Wheezing during work (OR 4.99, 95% CI 2, 29–20.89) and baseline FEV_1 (OR 1.49, 95% CI 1.05–2.20) were significantly and independently associated with being a reactor.

Longitudinal studies of bronchial responsiveness. One longitudinal study of bronchial responsiveness in the farming population has been published. Vogelzang *et al*. [111] studied changes in bronchial responsiveness over three years by means of histamine up to a dose of 16 mg/ml in 82 pig farmers consistently with symptoms, and 89 pig farmers consistently with no symptoms. The mean increase in responsiveness to histamine was 2.52 doubling dose concentration for PC_{10} and 1.63 doubling dose for PC_{20}. Long term average exposure to inhalable dust was associated with PC_{10} and exposure to ammonia, the use of wood shavings as bedding, and automated dry feeding were associated to PC_{20}. No association was found with the exposure of endotoxin.

Summary and remarks. The field of unspecific bronchial provocation is characterised by a heterogeneity in methods and measurements, thus making comparison between studies difficult. However, non-exposed control groups have been used in seven studies [1, 9, 13, 64, 91, 100, 123] and in three studies [1, 13, 123] the persons exposed were significantly more responsive than controls. In one study

[9], farmers with animal production were significantly more responsive than controls and farmers with no animal production. In three studies [64, 91, 100] no significant difference was observed in bronchial responsiveness. The prevalence of reactivity ($PC_{20} \leq 8$ mg/ml histamine) seems to be very high in subsamples of Danish farmers, between 95% (farmers with asthma) and 59% (farmers with no respiratory symptoms), n = 144 farmers [48] and 50% in swine farmers and 42% in dairy farmers, n = 181 farmers [94]. These prevalence data are much higher than data from 741 French dairy farmers where 10.3% were reactors (fall in $FEV_1 \geq 10\%$ after acetylcholine (1,200 mg) or increase in $FEV_1 > 10\%$ and 200 ml in subjects with a prechallenge $FEV_1 < 80\%$) [6]. The prevalence of reactivity ($PC_{10} \leq 16$ mg/ml histamine) in a random population sample of 2,156 subjects in the Netherlands was about 25% [89] and in a European Community Survey study of 13,161 subjects from 13 European countries, together with subjects from the USA, Australia and New Zealand [12] the prevalence of reactivity ($PD_{20} \leq 1$ mg methacholine) was 13%. In the Danish subsample the prevalence was 23.5%. Data regarding bronchial reactivity in farming populations are too inconsistent and sparse to evaluate any effect of farming exposure on bronchial reactivity, even though the findings from Denmark [12, 44, 48] indicate a higher prevalence of reactivity in farmers than in subjects from the city of Aarhus [12].

In both cross sectional- and longitudinal studies, exposure to ammonia, wood shavings as bedding, and automatic dry feeding [12, 114] have been found as risk factors associated with bronchial responsiveness. Cross-sectional studies alone have related age [44], baseline FEV_1 [6, 44], Pi alleles to α_1-antitrypsin [101], wheezing during work [6], pellet feeding and location of air exhaust [114] as risk factors. In a longitudinal study [12] farming was a risk factor.

LUNG FUNCTION IN FARMERS

Cross-sectional studies. In the last two decades several articles have been published addressing impaired lung function in subjects occupied in agriculture. Some of these studies have been designed with control groups and a sufficient number of participants. Mostly exposure in swine confinement buildings [13, 16, 29, 48, 121] has been described, but other farming occupations have been addressed such as dairy farming [18, 20, 38], dairy farming and horse raising [73], poultry breeding [25, 108, 124], grain farming [11, 41, 53, 67], other field harvests [95, 125], and one study has focused on farming students at the point of entering the trade [74].

Dosman *et al.* [29] found in their survey from Canada of 504 swine producers and 448 rural-dwelling non-farming controls, a lower FEV_1 and FVC in swine producers than controls, although there was a modest increase in FEV_1/FVC ratio among swine farmers, suggestive of a mixed restrictive/obstructive lung function impairment. In a Danish study [99] of 124 pig farmers and 57 dairy farmers a non-significant lower FEV_1 in pig farmers than in dairy farmers was found. The annual decline in FEV_1 was associated with pig farming (12 ml), smoking (23 ml/pack year) in addition to the age related decline of 32 ml. Canadian data [16] from a population comprising of 488 swine building workers, 216 non-farming neighbourhood controls showed a significant lower FEV_1/FVC among swine confinement workers than controls. Subjects working 3 hours or more in swine confinement buildings had more airflow obstruction than those working less hours. There was no difference in airflow obstruction between subjects working in swine confinement buildings only, and subjects working both in swine confinement buildings and dairy barns. Zejda *et al*. [121] studied younger Canadian farmers (249 swine producers, 251 grain farmers and 263 non-farming subjects). They found a significantly lower lung function in swine producers than in grain farmers, with measurements of FEV_1, FEV_1/FVC, FEF_{25-75} and forced expiratory flow at 50% and 25% FVC and non-farming subjects with measurement of FEV_1/FVC, FEF_{25-75} and forced expiratory flow at 50%. An indirect index of exposure was inversely related to FVC (significant) and to FEV_1 (borderline of significance). Decreased lung function was especially observed among swine producers aged 25–35 years. Unlike previous studies [16, 29, 48, 121] where lung function measurements tended to be lower in the exposed groups and especially among swine farmers, the lung function measurements were the same (FEV_1/FVC, FEF_{25-75}, PEF and MEF) as a study from Western France [95] involving 102 pig farmers, 51 dairy farmers and 51 non-farming referents from western France.

Two articles from the Doub province in France [18, 20] have analysed lung function in dairy farmers. The first study from 1989 [20] found lower values of FEV_1 and FVC in 250 dairy farmers compared to 250 controls. Data from the 1998 study [18] revealed a significantly lower FEV_1/VC ratio among 265 dairy farmers compared to the 145 non-exposed controls and the FEV_1/VC ratio like smoking was negatively correlated to dairy farming. Findings from France [18, 20] and data from England and Wales supports the assumption of an association between dairy farming and reduced lung function. Heller *et al*. [38] found in their study comprising of 428 farmers and 356 non-farming controls, a significant lower FEV_1/FVC ratio in subjects working regularly with dairy cattle and with silage compared to others farmers and controls. The FEF_{25-75} was also significantly reduced in regular dairy workers. In Croatian livestock farm workers [73] raising dairy cattle and horses FEV_1 and FVC were significantly lower only in non-smokers. No differences were observed for $FEF_{50\%}$ and $FEF_{25\%}$.

There have been several case reports and small scale studies published without a control group dealing with respiratory health in poultry farming, but few well-designed studies. Most of these reports have described the effect of the exposure on lung function. Addressing lung function in humans exposed to poultry breeding, Zuskin *et al*. [124] measured lung function in 343 poultry farm workers. In the poultry workers the FEV_1, FVC and FEF_{25} were significantly lower than predicted, and workers exposed for more than 20 years had lower lung function than subjects less exposed. Data from the USA [25] from a study of 257 poultry workers and 150 nonpoultry controls showed a significant effect of poultry work over the work shift on FEV_1, FVC and FEF_{25-75}. The mean FEV_1 decrease over the shift was highest for broiler workers. No baseline difference in FEV_1, FVC and FEF_{25-75} FEV_1, FVC was observed between poultry workers and controls. Lung function measured as FEV_1, FVC and FEF_{25-75} and PEF was analysed in a Norwegian study including 82 dairy farmers, 82 pig farmers, 74 sheep farmers and 20 poultry farmers [108]. No differences in measured lung function parameters between the groups were observed, but all values except for PEF were lower than values from the Norwegian reference population.

The respiratory effects of exposure to grain dust working in grain elevators in Canada have been described in many publications. The exposure measurements related to work in grain elevators indicate that the magnitude of the exposure has been substantially higher than exposure usually experienced for grain farmers [41]. The effect of grain exposure in farming was studied by Manfreda *et al*. [67]. The study population was 1,892 subjects in subgroups of current, former and never farmers. Nearly all current farmers were exposed to grain, on average 2 months a year. While smoking had a significant influence on respiratory health, there was no data supporting a grain dust exposure dependent reduction in lung function. In another Canadian study comprising 1,633 subjects [11], an effect of grain exposure on lung function was observed. A significant synergistic effect of smoking and grain exposure was obtained in women on FEV_1, FVC, MEFR, V'max 50 and V'max 25. No significant combined effect on lung function was observed in males. Data from Croatia [53] based on a study of 814 farm workers with no work related to breeding or livestock production revealed that FEV_1, FVC, $FEF_{50\%}$, $FEF_{25\%}$ were significantly lower in 738 male farming workers, compared to predicted normal values for the European population. In 76 females, no differences were observed for FEV_1, FVC was lower both in smokers and non-smokers while $FEF_{50\%}$ $FEF_{25\%}$ only were lower in non-smokers compared to predicted normal values for the European population.

Dust exposure from non-animal farming activities has been described as affecting respiratory health [51, 125]. Jorna *et al.* [51] studied the effect on lungs from exposure in organic dust from former sea terraces by sorting potatoes. 172 subjects (controls and exposed) were enrolled, of whom 72 were currently exposed and 16 were retired, but former exposed. There was a significant dose-relate dust exposure increase in annual decline i FEV_1 of 10.5 ml. In a study of 167 greenhouse workers [125] and 81 controls there were findings indicating impairment of lung function. Mean FEV_1 was lower in exposed compared to standard predicted values. FEF_{25} was significantly lower for subjects exposed more than 10 years than for subjects exposed for less. In young subjects [74] with few years of exposure in farming there was also a measurable difference in lung function. In 407 male controls the standardized FEV_1 and FVC residuals were higher than in 1,691 male farming students, both in non-smokers (0.21 and 0.24) *vs.* (-0.06 and -0.05) and smokers (0.29 and 0.33) *vs.* (-0.11 and 0.13) ($p < 0.032$). Bronchial hyperresponsiveness was the factor most strongly associated to reduced lung function.

Longitudinal data. Data concerning loss of lung function among subjects working in farming has been published during the last six years. Most of the studies have been of swine confinement exposure [43, 46, 57, 95, 98, 110, 112], but data from France [19, 68] and Finland [85] have been based on exposure in dairy farming. One longitudinal survey [98] has focused on the fate of lung function among subjects working as grain farmers.

Schwarz *et al*. [95] measured lung function in 168 swine confinement operators and 127 farming control subjects with no swine exposure during a two-year follow up period. FEV_1 and FEV_{25-75} were lower among swine confinement operators than control farmers, but their annual decline in lung function was not increased. However, work in swine confinement buildings, cross shift change in lung function % and total concentration of endotoxin were independent factors for increased loss of lung function in the multivariate model. In a Danish study with a five-year follow-up [46] the annual decline in FEV_1 was highest in pig farmers (73 ml), second highest in farmers with both pig and dairy production (60 ml), and lowest in farmers with no animal production (30 ml), but the differences were non-significant. The study population comprised three stratified subsamples (subjects with asthma n = 22, subjects with chronic bronchitis n = 42 and subjects with no respiratory symptoms n = 17) from 1,175 farmers. In a regression analysis, smoking, lung function and bronchial hyperresponsiveness were significant risk factors at start, and years of pig farming were of boarder line significance. A recent study from the same group [43] of 91 swine farmers and 38 dairy farmers participated in a seven-year follow-up study. The annual decline in FEV_1 but not in FVC was greater among swine farmers (53.8 ml) than dairy farmers (41.8 ml). For non-smokers, the increased annual decline in swine farmers was 17 ml compared to dairy farmers. In a four-year follow-up study from Canada [98] where 217 swine confinement workers, 218 grain farmers and 179 non-farming controls were enrolled, there was an increase in annual decline in FEV_1 and FVC for both swine confinement workers (26.1 ml and 33.5 ml) and grain farmers (16.4 ml and 26.7 ml) compared to non-farming controls. The annual decline in FEV_1 and FVC was significantly greater in both swine- and grain farmers compared to non-farming controls. The same group [57], in a study with a follow-up time of 4–5 years of 42 swine confinement building workers, found that the endotoxin level was a significant predictor of annual rate change for FEV_1 but not for FVC. Vogelzang *et al*. [112] found in their three-year follow-up study of 171 pig farmers, an annual decline in FEV_1 of 73 ml and in FVC of 55 ml, and an yearly loss of FEV_1 exceeded substantially the expected age-related decline of 29 ml. Analysing for occupational risk factors for annual loss in lung function use of quaternary ammonium compounds (additional 43 ml) as disinfectants and the use of an automated dry feed system (additional 28 ml) were associated with increased loss in FEV_1. Exposure data from the same study population [110] found a significant association between endotoxin exposure and annual decline in FEV_1. A factor two increase in exposure was associated with an extra annual decline of 19 ml in FEV_1. In a six-year follow-up study of 194 French dairy farmers and 155 non-farming controls [19], the annual decline in lung function was non-significantly higher in dairy farmers (FEV_1 32.8 ml, VC 43.1 ml) compared to controls (FEV_1 30 ml, VC 37.9 ml). Among male subjects aged 45 years or more, dairy farming was associated with accelerated loss in VC and FEV_1. The same group [68] studied the effect on lung function of drying fodder among dairy farmers in 113 barn drying farmers and 231 traditionally drying farmers in a five-year follow-up study. No effect on annual decline in lung function was observed from drying fodder. To study the effect of indoor feeding of cattle in Finland [85], a six-month longitudinal study was performed involving healthy non-smokers: 91 dairy farmers and 90 urban dwelling teachers. Significant decrease in lung function (PEF, FEV%, FVC), together with other spirometric indices were observed among dairy farmers compared to controls.

Summary and remarks. In eight [16, 18, 20, 29, 38, 51, 74, 121] of 12 studies on lung function involving a non-exposed control group [11, 13, 16, 18, 20, 25, 29, 38, 67, 51, 74, 121] baseline FEV_1 or FEV_1/FVC were significantly reduced in farmers. Main occupation was swine [16, 29, 121] dairy [18, 20, 38] and potatoes [51]. No differences in lung function were observed between swine-, dairy farmers and controls [13], poultry farmers and controls [25] and between grain farmers and controls [67, 111]. FEV_1 was lower in farmers in two studies [124, 125] and in one study [53] FEV_1, FVC, $FVC_{50\%}$, $FEF_{25\%}$ were lower in farmers comparing the measured values with predicted. In two studies [73, 108] FEV_1 and FVC were lower in farmers than in a referent population. There was a work shift reduction in FEV_1 and FVC in grain farmers [67], and reduced FEV_1/FVC was observed in female grain farmers who smoked [11]. These data suggest that several farming exposures might have an impact on lung function.

Data from the longitudinal studies suggest that working in swine confinement buildings increased the annual loss of FEV_1 by as much as 20–40 ml [43, 46, 98, 112]. Working in this environment for 20–30 years might, therefore, induce an extra loss in FEV_1 of 0.4–1.2 L, leading to airway obstruction of clinical importance. Exposure to dairy- [19, 43] and grain farming [98] does not seem to influence FEV_1 to the same extent as exposure from tending pigs.

Smoking, lung function and bronchial hyperresponsiveness [46], together with exposures to disinfectants, automated dry feed system [25] and endotoxin [57, 110] have been described as risk factors for increased annual decline in lung function.

CONCLUSION

During the last two decades the number of studies focusing on exposure respiratory diseases and lung function in farming populations in temperate zones, have been numerous. However, several studies suffer from methodological weaknesses and findings in the studies might incorrectly contradict each other, due to heterogenity in sampling time, measurements technique, equipment, and in diagnostic criteria. These observations indicate that general conclusions should be drawn with care. Despite these limitations, some patterns in the data suggest some concluding remarks and pinpoints other fields for further research.

Working in animal housings can be associated with exposure to organic dust, bacteria, moulds, endotoxin and ammonia in concentrations which when inhaled can induce cellular and immunological responses that can result in respiratory diseases. Data suggests that working in poultry housings is associated to higher exposure to dust, both in the total and in the respirable fraction, compared to swine- or cow housings. No such patterns have been measured for moulds, while bacteria counts and ammonia measurements indicate a higher exposure in poultry housings than swine- and cow housing. Data concerning exposure to endotoxin have shown great dispersion, with several series measuring concentrations high enough to induce health effects. The exposure assessments from North America seems to be higher than those from Europe, and no convincing differences in exposure to endotoxin between the different animal housings have been observed.

Of the common inhalant allergens, sensitisation to mites seems to be the most prevalent in farming populations, and in Scandinavia *Lepidoglyphus Destructor* is the most frequent species. There are signs indicating that working exposure in farming might influence the domestic area, and there might be a protective effect of being raised on a farm regarding sensitisation to common inhalant allergens and allergic diseases.

Chronic bronchitis seems to be increasing in farming populations, and longitudinal studies suggest that chronic bronchitis is a work-related disease in farmers. Data concerning asthma are less uniform, and no pattern in the data from the cross-sectional studies indicates an increased prevalence of the disease in farming populations, and findings regarding bronchial reactivity are too sparse and inconsistent to evaluate the effect of farming exposure. Several risk factors have been described for the different clinical conditions, but age is shared for all three clinical manifestations. Male gender and atopy, together with environmental exposures such as smoking, pig farming, and animal production, are common risk factors for both asthma and chronic bronchitis. Being a farmer is a risk factor for chronic bronchitis as well as for bronchial responsiveness. In both cross-sectional and longitudinal studies, atopy, smoking and swine farming have been found as risk factors for chronic bronchitis, and exposure to ammonia, wood shavings as bedding, and automatic dry feeding have been found as risk factors for bronchial responsiveness.

Lung function measured as FEV_1 or FEV_1/FVC seems to be reduced in farmers compared to controls, and longitudinal studies indicate an increased annual loss in FEV_1 in farmers, especially in pig farmers. The increased annual decline in lung function has been associated with lung function, bronchial hyperresponsiveness, together with environmental exposures, such as smoking, disinfectants, automatic dry feeding systems and endotoxin.

Few studies focusing on respiratory symptoms and lung function in farming populations have precise and accurate exposure assessments, and few studies focusing on exposure measurements inside animal houses have information on human health effects. Hence, it is difficult to establish dose-response relationships. More studies combining measurements of exposure to the effect are needed. Realising that these studies are costly, well-constructed exposure matrices for relevant exposure ought to be tried and associated to health outcome in order to conduct more precise and exact analyses regarding association between health outcome and environmental exposure. A great challenge lies in further studies on the possible protective effect of being raised on a farm regarding sensitisation and allergic diseases, both concerning what kind of environmental components are responsible for this protective effect, and how long this effect will last. Studies analysing for this possible environmental protective effect on the annual loss in lung function will also be of considerable interest. Few studies have raised the question concerning gene environment interaction, and continuous effort in clarifying this issue will further add to the understanding of how equal exposure conditions lead to different health outcomes. Well-designed longitudinal studies in farming populations are needed with respiratory symptoms and lung function as the objective combined with good exposure assessments. Those which have been published are few, and so far none have addressed asthma.

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