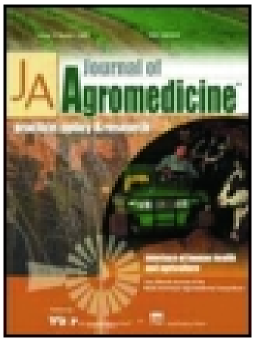

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Synergistic Effects of Dust and Ammonia on the Occupational Health Effects of Poultry Production Workers

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ABSTRACT. Objective. As production methods for livestock and poultry moved towards large industrial-scale confinement facilities, the occupational health community reported risks for respiratory illnesses in workers. Likely, greater risks for respiratory disease will occur with the continuing trend towards full-time confinement workers, who inspire a combination of bioaerosols, particulates, and gases.[1-3] Although there have been numerous studies on the individual health effects of air contaminants inside confined animal production facilities, there have been no reports on the effects of combined exposures. The objective of this study was to investigate the combined health effects of air contaminants on poultry production workers.

Sample Population. Two hundred and fifty-seven poultry production workers participated in this study. The workers represented various areas of the poultry industry, including turkey growing, broiler production, egg laying, and unloading/shakeling in poultry processing. Worker procedures pulmonary function testing was conducted before and after a

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four-hour work shift. The work environment was assessed for total and respirable dust, ammonia, endotoxin and CO_2. The relationship of simultaneous total dust and ammonia exposures was examined by correlation, logistic modeling, and synergy index calculations.

Results. Synergy between ammonia levels and airborne dust explained up to 43% and 63% of the decline (respectively for Forced Expiratory Volume (FEV) in one second and Forced Expiratory Flow ([FEF_{25-75}]) in pulmonary function over the work shift. Furthermore, assessing the synergy index indicated the combined effect of dust and ammonia is from 53 to 156% (greater combined than individually). The proportion of health effect due to synergy is 35%-61%.

Conclusions. Synergy of simultaneous dust and ammonia exposures in a working environment raises the question of redefining exposure limits for organic dust and ammonia when workers are exposed simultaneously to these substances.

Clinical Relevance. Control of both dust and ammonia in livestock facilities is extremely important. Lack of control of both these contaminants will increase the risk of respiratory dysfunction to all exposed to this environment, including workers and veterinarians.

KEYWORDS. Dust, ammonia, synergy, health effects, poultry, working environment

INTRODUCTION

Approximately 700,000 persons work in animal confinement facilities in the United States[4] with an estimated 80,000 full-time equivalent poultry farmworkers.[5] Because contract raising of poultry for large integrators is commonly undertaken as a family endeavor to supplement household income, the total numbers of exposed persons (including men, women, and children with part-time employment) is much greater than the estimated 80,000 full-time equivalents.

In the late 1950s, poultry production evolved into an industrial-style system, utilizing confinement operations. Efficiency in production has been highly emphasized in this industry. However, the health of exposed workers has been largely overlooked by the industry, even though research has confirmed the negative impacts of poultry house exposures on workers' respiratory health. Poultry workers have a high prevalence of acute, work-related symptoms including cough, phlegm, eye irritation, dyspnea, chest tightness, fatigue, nasal congestion, wheezing, sneezing, nasal discharge, headache, throat irritation, and fever.[3,6-13] Chronic symptoms of cough, phlegm, wheezing, dyspnea, and chest tightness have also been documented in poultry production workers and poultry processing workers.[12-14]

Patterns of lung function change in poultry workers are suggestive of primary obstructive disorders with less consistent indication of restrictive pathology. Baseline measures of FVC and FEV_1 were found to be significantly lower than normal predicted values in chicken breeders.[15] Cross-shift decreases in FEV_{11} were more pronounced at worksites handling chickens where dust and endotoxin levels were high.[7] A study of live-hang shacklers (the first stage of poultry processing), revealed small but significant cross-shift decreases in FVC and FEV_1.[10,11] Significant cross-shift declines in FEV_1 and FEF_{25-75} were detected in a study of turkey, broiler, and layer workers.[16-18] Chicken catchers were found to have significant decreases in FEV_1 and FVC over the work shift.[12] Likewise, significant cross-shift declines in FEV_1 and FVC were observed in turkey workers exposed to high concentrations of dust, endotoxin, ammonia, and bacteria.[3] Poultry growers and catchers exhibited significantly lower baseline measures of FEV_1, FVC, and FEF_{25-75} than normal predicted values.[13]

Histopathology and *in vitro* studies provide additional evidence of elevated risk for obstructive respiratory disease in poultry confinement workers. Bronchial biopsies of chicken growers revealed thickening of the basement membrane with migration of neutrophils and eosinophils into airway epithelium, suggesting a permeability defect and acute inflammation.[19] An *in vitro* study of the effect of poultry dust extract on contractility of guinea pig tracheal rings demonstrated that poultry antigens are capable of inducing nonimmunological airway constriction.[13,20]

In addition, allergic alveolitis, [6,21,22] psittacosis,[23] and occupational asthma[24-26] have been implicated sporadically in association with occupational poultry exposures. High prevalences of precipitating antibodies and skin sensitivity to poultry-derived antigens have been found in poultry workers, but have poor correlation with symptoms and pulmonary function.[6,8,10,11,15,27,28]

Environmental studies in poultry facilities have quantified ammonia, dust, bacteria, and endotoxin in ranges where health effects have occurred in other occupational settings.[2,3,12,29-33] Airborne molds have been detected in high numbers, but concentrations of hydrogen sulfide, methane, carbon monoxide, carbon dioxide, and nitrogen dioxide have been well below occupational exposure limits in most poultry facilities.[7,30,31,33,34]

Symptoms and patterns of airflow obstruction similar to poultry workers have been documented in workers occupationally exposed to organic dusts from a variety of sources including swine confinement, dairy barns, grain handling, wool sorting, animal feed production, vegetable fibers processing (cotton, flax, sisal, hemp, jute), sewage and compost handling, and wood dusts.[1,13,35,36]

Dusts in animal confinement facilities are organically derived, heterogeneous mixtures arising from feed, feces, and animal dander and hair. Laborers in confinement housing are exposed to these aerosolized contaminants including feed additives, broken feather parts, dried ammonia, viable and nonviable bacteria, bacterial endotoxins, glucans, molds, and fungal spores.[2,7,29,38] Inhalation of confinement dusts can result in adverse inflammatory, toxic, or allergic effects, including bronchitis, asthma, an inflammatory-based asthmatic-like condition, organic dust toxic syndrome, a toxic alveolitis, rhinitis, mucus membrane irritation, and allergic alveolitis.[30,39] The most common adverse respiratory effect is the development of bronchitis, with defining symptoms of cough and phlegm.[4,40] Smoking has been found to exacerbate symptoms and pulmonary disfunction.[17]

Individual response is highly variable depending on individual susceptibility and concurrent cardiopulmonary disease, as well as aerosol composition, particulate size, antigenicity, duration of exposure, and concentration.[41] Components in the confinement environment most likely contributing to adverse respiratory effects include dust, endotoxin, and ammonia.[18] Dust can act as a nonspecific irritant by overwhelming the clearance mechanisms of the respiratory tract. Endotoxins, derived from the lipopolysaccharide portion of gram-negative bacterial cell walls, are capable of macrophage activation, neutrophil recruitment, complement activation, and histamine release.[42,43] Ammonia, a by-product of bacterial action on animal or human excreta, is adsorbed to dust particles, inhaled, and distributed through the respiratory tree to exert effects as an alkaline respiratory irritant.[38]

The extent of exposures in animal confinement facilities is variable depending on age and species of animal confined, waste management practices, feed composition, methods of feeding, ventilation, season, building structure, flooring materials, humidity, restraint in pens or cages, type of bedding, frequency of handling, animal density, and general management skills.[18,41]

The fecal portion of confinement dusts is generally concentrated in small, highly respirable (less than 5 μm diameter) particles, constituting a respiratory threat from airways through alveoli. Larger particles of feed and feather origin are deleterious primarily to the upper airways.[41]

OSHA has established a Permissible Exposure Limit (PEL) for "Particulates Not Otherwise Classified" at a time-weighted average (TWA) over an 8-hour day as 15 mg/m^3. The OSHA TWAs for respirable particles and ammonia are, respectively, 5 mg/m^3 and 50 parts per million. Threshold limit values (TLVs) established by the American Conference of Governmental Industrial Hygienists[43] (ACGIH) include 10 mg/m^3 for nuisance dusts, 4 mg/m^3 for grain dusts, 3 mg/m^3 for respirable dusts, and 25 ppm for ammonia.[44,45] However, these limits may be too high for animal confinement where a combination of biologically active agents can harmonize to produce respiratory and systemic effects.

Multiple agents, multiple etiologies, and the potential for nearly limitless interactions make thorough evaluation of occupational organic dust exposures a staggering task. The assignment of unquestionable causality to a single agent for a single dysfunction in confinement facilities is unlikely at best. Furthermore, prior analysis of this data set revealed prominent dose-response relationships between increasing environmental dust, ammonia, and endotoxin concentrations with corresponding cross-shift declines in worker lung function. Specific threshold concentrations were defined including: total dust, 2.4 mg/m^3; respirable dust, 0.16 mg/m^3; total endotoxin, 100 EU/m^3; respirable endotoxin, 0.35 EU/m^3; and ammonia, 12 ppm.[46] As health effects to poultry workers from exposure to both dust and ammonia were less than half the published ACGIH TLVs, we were interested in investigating possible interactions between these substances.

MATERIALS AND METHODS

Study Design

Study Population

Two hundred and fifty-seven poultry workers (women 30%, men 70%) were recruited for study, including 124 turkey growers/loaders, 92 egg producers, 26 broiler growers, and 15 shacklers. Poultry and egg producers were recruited for participation from the complete list of members of the Iowa Turkey Federation, Iowa Egg Council, 1985 Poultry Industry Directory, and the 1985 Who's Who in the Egg and Poultry Industries. A non-exposed blue-collar comparison group (42% women, 58% men) was assembled from the complete list of Iowa City postal workers (111) and an area electronics assembly plant workers (39).

Medical Evaluation

Trained interviewers and technicians conducted health interviews and medical evaluations on-site. The standardized American Thoracic Society (ATS) questionnaires,[47] with additional questions to assess occupational and exposure histories, were administered by trained interviewers. Pulmonary function tests were conducted by a trained research assistant using a Spirotech S500 spirometer (Ohio Instruments). ATS guidelines for spirometry were followed.[48] Pulmonary function tests were performed before and after the work shift to assess cross-shift changes, with a minimum of two hours of exposure required (the usual exposure period was four hours).

Environmental Evaluation

Environmental studies consisted of collection and quantification of personal samples of total dust, respirable dust, total endotoxin, respirable endotoxin, and ammonia. Ammonia exposures were quantified by attaching passive diffusion tubes to poultry workers during their work shift. Dust samples were collected gravimetrically on 5 μm pore, 37 mm low ash PVC membrane filters housed in 2-stage closed cassettes in line with personal air sampling pumps (Gelman, Inc.), utilizing flow rates of 1-2 liters per minute. Probed respirators (3M 9920) were utilized for in-mask sampling of total dust in 34 workers who usually wore respiratory protection. Respirable samples were collected by incorporating MSA cyclone pre-selectors into sampling trains, with flow rates of 1.7 liters per minute. Respirable dust samples were not collected for the 34 workers wearing respiratory protection because of the cumbersome nature of attaching two sampling devices to the masks. The QCL1000 endpoint method of the Limulus amebocyte lysate assay was utilized for endotoxin analysis (NIOSH).

Statistical Analysis

SAS software was used to perform statistical analysis. P values less than or equal to 0.05 were considered statistically significant unless otherwise noted. Univariate procedures were utilized to yield descriptive statistics. Histogram plots were examined to evaluate normality of distributions because log transformed data were not normally distributed. Data were not log transformed for analysis. Non-parametric Spearman correlation coefficients were calculated to determine relationships (1) among environmental exposures and (2) between environmental exposures and lung function changes.

Interactions between the exposures of ammonia and total dust, and their combined effect on cross shift decline in FEV and FEF_{25-75} were evaluated by comparing effects of varied concentrations of ammonia and dust, in combination, on work shift change in pulmonary function. These relationships were examined by dividing the environmental variables into high and low concentrations (> median = "high"; < median = "low") and entering the following variables into logistic models: low total dust, high total dust, low ammonia, high ammonia, and interaction terms of low dust·low ammonia, low dust·high ammonia, high dust·low ammonia, and high dust·high ammonia. Backward elimination procedures were performed to determine which variables would be retained as significant contributors to the models.

In addition, the combination terms of low dust/low ammonia, low dust/high ammonia, high dust/low ammonia, and high dust/high ammonia (as well as control variables) were simultaneously forced into regression models for predicting 3%, 5% and 10% cross-shift in decline of FEV and FEF 25-75. Odds ratios and 95% confidence intervals were calculated for the combination terms of 3%. Finally, calculations were made for the Synergy Index (S) and the proportion of pulmonary function change attributable to interaction [AP*(AB)].[49] The Synergy Index is defined as "the ratio of the observed effect with combined exposures to that effect expected with independently acting causes operating jointly,"[48,49] with effect defined as excess risk. If the observed risks for combined ammonia and dust exposures are greater than the risks based on the sum of their individual effects, positive interaction (synergy) is said to occur.

RESULTS

Table 1 addresses the demographic characteristics of poultry workers and controls. The mean number of years worked in the poultry industry was 9.7 (sd = 9.1). Race was uniform (99.8% Caucasians).

Earlier analysis had shown that poultry work status was significantly associated with a work shift decline in FEV_1 and FEF_{25-75}, after adjusting for current smoking status.[17]

Table 2 summarizes personal environmental measures including total dust, respirable dust, total endotoxin, respirable endotoxin, and ammonia. Ranges

TABLE 1. Demographic Characteristics of Study Subjects*

	Poultry Workers (n = 257)	Controls (n = 150)
Male	77%*	58%
Age	38.8 14.2†	42.1 9.5
Education (years)	12.2 2.1	13.1 2.0
Smoking Status (%)		
Never	52.9%	42.67%
Former	19.1%	30.67%
Current	28.0%	26.70%

*Categorical values are expressed as percentages
†Continuous variables are expressed as mean standard deviation

for the environmental variables were as follows: total dust (0.02-81.33 mg/m^3), respirable dust (0.01-7.73 mg/m^3), total endotoxin (0.24-39,166.89 EU/m^3), respirable endotoxin (0.35-693.99 EU/m^3), and ammonia (0-75 ppm).

Spearman/Environmental Correlationss

Table 3 summarizes Spearman correlations between environmental variables. Highly significant (e.g., $p < 0.0001$), moderately strong (e.g., $r = 0.4$-0.8) Spearman correlation coefficients were observed between all combi-

TABLE 2. Environmental Exposures of Poultry Workers

		X*	S.D.**
Total Dust (mg/m^3)	n = 238	6.5	7.8
Respirable Dust (mg/m^3)	n = 210	0.63	0.98
Total Endotoxin (EU/m^3)	n = 236	1589.1	3394.1
Respirable Endo (EU/m^3)	n = 210	58.9	97.3
Ammonia (ppm)	n = 174	18.4	17.5

*Mean
**Standard deviation

TABLE 3. Spearman Correlation Coefficients Between Environmental Exposure Variables

	Total Dust	Respirable Dust	Total Endotoxin	Respirable Endotoxin	Ammonia
Total Dust	1.000* (0.0000)†	0.539 (0.0001)	0.590 (0.0001)	0.466 (0.0001)	0.178 (0.0190)
Respirable Dust	0.539 (0.0001)	1.000 (0.0000)	0.461 (0.0001)	0.562 (0.0001)	0.007 (0.9352)
Total Endotoxin	0.590 (0.0001)	0.461 (0.0001)	1.000 (0.0000)	0.646 (0.0001)	0.095 (0.2125)
Respirable Endotoxin	0.466 (0.0001)	0.562 (0.0001)	0.646 (0.0001)	1.000 (0.0000)	0.170 (0.0427)
Ammonia	0.178 (0.0190)	0.007 (0.9352)	0.095 (0.2125)	0.170 (0.0427)	1.000 (0.0000)

*Upper number denotes r-value
†Lower number denotes p-value

nations of total dust, respirable dust, total endotoxin, and respirable endotoxin. Ammonia was weakly ($r < 0.2$) but significantly correlated to only two particulate variables (total dust and respirable endotoxin).

Spearman correlation coefficients between environmental variables and cross-shift changes in lung function (Table 4) revealed that cross-shift decrements in FEV_1 were weakly but significantly correlated to all environmental variables except ammonia. Cross-shift decrements in FEF_{25-75} were weakly and significantly correlated with total dust and total endotoxin. Cross-shift decrements in FEV_1 and FEF_{25-75} were moderately ($r = 0.66$) and significantly correlated.

Interaction Evaluation

Total dust and ammonia were studied for interaction evaluation because total dust and ammonia were the only environmental variables that contributed significantly to the backward elimination models examined. Furthermore,

TABLE 4. Spearman Correlation Coefficients Between Environmental Exposure Variables and Cross-Shift Changes in Lung Function

	% Cross-Shift Decline	
	FEV_1	FEF_{25-75}
Total Dust	0.265* (0.0001)†	0.275 (0.0001)
Respirable Dust	0.155 (0.0253)	0.122 (0.0785)
Total Endotoxin	0.193 (0.0030)	0.201 (0.0020)
Respirable Endotoxin	0.157 (0.0232)	0.085 (0.2198)
Ammonia	0.081 (0.2885)	0.058 (0.4443)
FEV_1	1.000 (0.0000)	0.658 (0.0001)
FEF_{25-75}	0.658 (0.0001)	1.000 (0.0000)

*Upper number denotes r-value
†Lower number denotes p-value

considering work place monitoring, both total dust and ammonia can be relatively easily and economically accessed (e.g., MiniRam Particle Counter and Colorimetric Tube Indicators).

To determine if interactive effects were occurring, the distributions of ammonia and total dust measures were divided at their medians into "high" or "low" categories. Predictor variables entered into logistic models included low total dust, high total dust, low ammonia, high ammonia, and interaction terms of low dust·low ammonia, low dust·high ammonia, high dust·low ammonia, and high dust·high ammonia (all relative to the non-exposed group). High total dust contributed significantly to all logistic models predictive of 3%, 5%, and 10% cross-shift declines in FEV_1 and FEF_{25-75}. Low total dust contributed significantly to the model, predicting a 5% or greater cross-shift decline in FEV_1. Ammonia and the interaction terms did not significantly contribute to the models.

To further determine if any evidence of interaction was occurring, logistic regression analysis was performed with forcing the variables low dust/low ammonia, low dust/high ammonia, high dust/low ammonia, and high dust/high ammonia into the models (controlling for age, years worked in poultry industry, gender, smoking status, and education). Dependent variables were the observed 3%, 5%, and 10% cross-shift declines in FEV_1 and FEF_{25-75}. Odds ratios and 95% confidence intervals for the combination terms can be viewed in Tables 5-9. The high (dust)/high (ammonia) categories consistently have statistically significant odds ratios that are greater than any other combination

TABLE 5. Odds Ratios and 95% Confidence Intervals for Total Dust and Ammonia Combination Terms Predictive of 3% or Greater Cross-Shift Declines in FEV_1‡

High Total Dust* High Ammonia 5.947† (2.207, 16.027)	Low Total Dust High Ammonia 1.582 (0.508, 4.924)
High Total Dust Low Ammonia 3.244 (1.135, 9.270)	Low Total Dust Low Ammonia 1.492 (0.554, 4.016)

*Total dust and ammonia categorized as "High" or "Low" based on a median split
† Odds Ratios and 95% Confidence Intervals were calculated considering ammonia and total dust exposures simultaneously (high dust/high ammonia, high dust/low ammonia, low dust/high ammonia, low dust/low ammonia), relative to non-exposed workers
‡ Results controlled for age, years worked in poultry industry, gender, smoking status, and education

TABLE 6. Odds Ratios and 95% Confidence Intervals for Total Dust and Ammonia Combination Terms Predictive of 5% or Greater Cross-Shift Declines in FEV_1‡

High Total Dust* High Ammonia 12.145† (3.080, 47.890)	Low Total Dust High Ammonia 5.806 (1.285, 26.241)
High Total Dust Low Ammonia 6.288 (1.369, 28.884)	Low Total Dust Low Ammonia 4.903 (1.228, 19.571)

*Total dust and ammonia categorized as "High" or "Low" based on a median split
† Odds Ratios and 95% Confidence Intervals were calculated considering ammonia and total dust exposures simultaneously (high dust/high ammonia, high dust/low ammonia, low dust/high ammonia, low dust/low ammonia), relative to non-exposed workers
‡ Results controlled for age, years worked in poultry industry, gender, smoking status, and education

TABLE 7. Odds Ratios and 95% Confidence Intervals for Total Dust and Ammonia Combination Terms Predictive of 3% or Greater Cross-Shift Declines in FEF_{25-75}‡

High Total Dust* High Ammonia 6.805† (2.702, 17.137)	Low Total Dust High Ammonia 1.199 (0.461, 3.116)
High Total Dust Low Ammonia 3.069 (1.197, 7.866)	Low Total Dust Low Ammonia 1.880 (0.836, 4.229)

*Total dust and ammonia categorized as "High" or "Low" based on a median split
† Odds Ratios and 95% Confidence Intervals were calculated considering ammonia and total dust exposures simultaneously (high dust/high ammonia, high dust/low ammonia, low dust/high ammonia, low dust/low ammonia), relative to non-exposed workers
‡ Results controlled for age, years worked in poultry industry, gender, smoking status, and education

category (high/low, low/high, and low/low). Furthermore, high dust/low ammonia exposures consistently have greater odds ratios than low dust/high ammonia.

Estimates of the Synergy Index (S) and the proportion of effect due to synergy [AP*(AB)] were then calculated from ORs observed in Tables 5-9. The Synergy Index is an indication of the level of interaction between two vari-

TABLE 8. Odds Ratios and 95% Confidence Intervals for Total Dust and Ammonia Combination Terms Predictive of 5% or Greater Cross-Shift Declines in $FEF_{25\text{-}75}$‡

High Total Dust* High Ammonia 6.554† (2.600, 16.524)	Low Total Dust High Ammonia 1.835 (0.689, 4.888)
High Total Dust Low Ammonia 3.797 (1.440, 10.012)	Low Total Dust Low Ammonia 1.719 (0.720, 4.105)

*Total dust and ammonia categorized as "High" or "Low" based on a median split
† Odds Ratios and 95% Confidence Intervals were calculated considering ammonia and total dust exposures simultaneously (high dust/high ammonia, high dust/low ammonia, low dust/high ammonia, low dust/low ammonia), relative to non-exposed workers
‡ Results controlled for age, years worked in poultry industry, gender, smoking status, and education

TABLE 9. Odds Ratios and 95% Confidence Intervals for Total Dust and Ammonia Combination Terms Predictive of 10% or Greater Cross-Shift Declines in $FEF_{25\text{-}75}$‡

High Total Dust* High Ammonia 7.259† (2.609, 20.199)	Low Total Dust High Ammonia 1.239 (0.347, 4.423)
High Total Dust Low Ammonia 3.262 (1.078, 9.871)	Low Total Dust Low Ammonia 2.642 (0.979, 7.128)

*Total dust and ammonia categorized as "High" or "Low" based on a median split
† Odds Ratios and 95% Confidence Intervals were calculated considering ammonia and total dust exposures simultaneously (high dust/high ammonia, high dust/low ammonia, low dust/high ammonia, low dust/low ammonia), relative to non-exposed workers
‡ Results controlled for age, years worked in poultry industry, gender, smoking status, and education

ables relative to the expected effects under the assumption of independence. AP*(AB) is the proportion of the interactive effect due to synergy of the dual exposures. If risks for combined exposures of high dust and high ammonia are greater than their added individual risks, then positive interaction (synergy) is occurring. The following equations were used to determine the Synergy Index and AP*(AB) for high dust/high ammonia exposures for 3%, 5%, and 10%

cross-shift declines in FEV_1 and $FEF_{25\text{-}75}$. Note: Odds Ratios (OR) were used as an approximation of relative risk (RR).

$$S = \frac{RR(AB) - 1}{RR(A\bar{B}) + RR(\bar{A}B) - 2}$$

and

$$AP^*(AB) = \frac{RR(AB) - RR(A\bar{B}) - RR(\bar{A}B) + 1}{RR(AB) - 1} = \frac{S - 1}{S}$$

Where:

RR(AB) = OR for high dust and high ammonia exposures

$RR(A\bar{B})$ = OR for high dust but low ammonia exposures (as an approximation for high dust/no ammonia since there were no observations made)

$RR(\bar{A}B)$ = OR for low dust but high ammonia exposures (as an approximation for no dust/high ammonia since there were no observations where dust was absent)

S = 0 if "causes" neutralize one another
S = 1 under additivity ("causes" acting independently)
S > 1 if OR observed for joint high exposures is greater than predicted based on additivity (synergism)
S < 1 if OR observed for joint high exposures is less than predicted based on additivity (antagonism)
S = infinity if "causes" produce no effect individually, but jointly produce an effect
AP*(AB) = The proportion of % FEV_1 or $FEF_{25\text{-}75}$ decline due to high dust and high ammonia that is attributable to their interaction (Rothman, 1986)

Substituting ORs (from Tables 5-9) for high dust/high ammonia [RR (AB)], high dust/low ammonia [$RR(A\bar{B})$], and low dust/high ammonia [$RR(\bar{A}B)$] exposure categories into the above equations resulted in S = 1.75 and S = 1.10 for 3% and 5%, respectively, cross-shift declines in FEV_1. The interpretation here is that the combined effects of dust and ammonia were 75% greater (at 3% FEV_1 decline) or 10% greater (5% FEV_1 decline) relative to their individual effects. AP*(AB)s were determined to be 0.43 and 0.09 for 3% and 5%

cross-shift declines in FEV_1. In other words, the synergy of the combined exposures account for 43% or 9% of the observed FEV_1 decrements.

Determination of the Synergy Index for cross-shift declines in FEF_{25-75} resulted in S = 2.56, S = 1.53, and S = 2.50 for corresponding 3%, 5%, and 10% changes. In other words, the combined effects of ammonia and dust are from 53% to 156% greater than their expected individual effects. Also, the AP*(AB)s for 3%, 5%, and 10% cross shift declines were determined to be 0.61, 0.35, and 0.60, respectively, indicating the proportion of total effects due to synergy is from 35% to 61%. Summary of these results are seen in Table 10.

DISCUSSION

Demographic Characteristics

Poultry workers had more respiratory symptoms and significantly larger cross-shift declines in FEV_1 and FEF_{25-75} compared to controls[38] suggesting that environmental exposures of poultry workers were capable of inducing respiratory disfunction.

Respiratory Function

Cross-shift declines in FEV_1 and FEF_{25-75} have been noted frequently in animal confinement studies and are indicative of obstructive respiratory disor-

TABLE 10. Summary of Strength of Dust-Ammonia Synergy (Synergy Index, S) and Proportion of Effect (Decline in Pulmonary Function) Due to Synergy [AP* (AB)]

Pulmonary Function	S[1]	AP*(AB)[2]
FEV_1 Decline		
3%	75%	43%
5%	10%	9%
10%	–	–
FEF_{25-75} Decline		
3%	156%	61%
5%	53%	35%
10%	150%	60%

[1] % greater effect of dust-ammonia in combination
[2] Proportion of effect due to synergy

ders.[1,6,50] The mean percent cross-shift decline in FEV_1 was 0.02% in controls compared to 1.10% in poultry workers. Mean cross-shift changes in FEF_{25-75} were a 2.10% increase in controls compared to a 1.50% decline in exposed workers (a net difference of −3.6%).

Spearman/Environmental Correlations

The fact that moderately strong correlations exist between all combinations of total dust, respirable dust, total endotoxin, and respirable endotoxin is advantageous for implementing environmental controls, because any control method reducing one of these contaminants will likely reduce all of the above contaminants. For example, strong correlations imply that effective total and respirable dust control will simultaneously result in endotoxin reduction. Because ammonia was only weakly correlated with total dust, ammonia control measures are independent of dust control. Also, the fact that neither total endotoxin nor respirable dust was correlated with ammonia probably reflects the variability between different poultry worker environments evaluated. Specifically, previous results revealed that caged layer facilities (compared to broiler houses, turkey houses, shacklers, and loaders) had the highest ammonia but the lowest respirable dust and total endotoxin concentrations.

Interaction Evaluation

Although no dust·ammonia interactive terms remained as significant contributors in logistic models, additive interactions can be masked by logistic regression techniques (because of the multiplicative nature of product terms).[49] The fact that only high total dust contributed significantly to all models where 3%, 5%, and 10% cross-shift declines in FEV_1 and FEF_{25-75} were the dependent variables suggests that total dust acts as a cause or surrogate marker capable of predicting adverse effects. This indicates that total dust should be the primary environmental parameter targeted for control in poultry confinement until specific causal subcomponents have been elucidated.

In viewing Tables 5-9, the fact that high total dust/high ammonia categories consistently had statistically significant odds ratios that were greater than any other combination category (high/low, low/high, and low/low) is indicative of interactive effects between ammonia and total dust. In addition, the fact that high dust/low ammonia exposures invariably had greater odds ratios than low dust/high ammonia suggests that dust is the more important exposure variable, conforming with results of backward elimination methods. Because odds ratios for high dust/high ammonia exposures consistently exceeded the sums of odds ratios for high dust/low ammonia and low dust/high ammonia categories, further investigation into interactive effects was conducted, utilizing the Synergy Index.

The fact that the Synergy Index for high dust/high ammonia exceeded one indicates that high dust/high ammonia exposures exert positive synergistic effects. The synergy values suggest interactive effects between high dust and high ammonia that are greater than additive. The AP*(AB)s quantified the degree of synergy (beyond additive) 9-43% of the effect for FEV_1 decrements and 35-61% of cross-shift declines in FEF_{25-75}.

Even though the synergistic effect calculated here is substantial, the true value may actually be higher because Odds Ratios used to calculate the Synergy Index were based on low dust/high ammonia and high dust/low ammonia (rather than no dust/high ammonia and high dust/no ammonia) exposure categories; the effect of the interaction is likely underestimated.

For occupational health issues, departures from additivity of effects (as opposed to multiplicative effects) of multiple exposures are the relevant focus. It is apparent that occupational pulmonary effects depend on the extent to which high levels of dust and ammonia exposures occur simultaneously. This knowledge is contradictive to current ACGIH methods recommended to calculate exposure limits in multiple exposures to assume an additive effect, suggesting if one substance was at half the TLV, the second substance cannot reach above half its TLV. The data in this paper show that dust and ammonia interaction is greater than additive. From an occupational health standpoint, one or other of the two substances should be reduced to very low levels, or both substances should be reduced simultaneously.

The synergy between dust and ammonia is logical from a biological standpoint because ammonia is dependent on adsorption to particulates[51,52] for distribution to the lower respiratory tract. Upon deposition, adsorbed ammonia and biologically active subcomponents of the particulate matter can exert direct inflammatory effects or stimulate alternate pathways leading to bronchoconstriction.

Summary

The combination of total dust and ammonia in poultry housing was found to have greater than additive health effects as measured by cross-shift declines in lung function. Therefore, it is important to develop control measures to reduce both dust and ammonia. This factor also explains why one cannot use OSHA published values of exposure limits in livestock confined animal feeding feed operations for dust (15 mg/m^3) and ammonia (50 ppm). This further validates previous studies,[1,16,53] that exposure limits for these combined substances in livestock buildings should be much lower (as suggested 2.5 mg dust/m^3 and 7 ppm ammonia).

Control Measures

Because the poultry industry is vertically integrated, and controlled by a few major companies, environmental control efforts are feasible from a management perspective. Short-term solutions to exposure reduction include improving ventilation, use of respiratory protective devices, humidity control, addition of ammonia stabilizers to litter, power washing buildings between production cycles, use of dust binders such as aerosolized vegetable oils, electrostatic precipitation of dust, use of extra oil/fat in feed, and use of high oil corn as a feed component.[54]

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