Occupational factors and reproductive outcomes among a cohort of female veterinarians

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Objective—To estimate absolute and relative risks of preterm delivery (PTD) and small-for-gestational-age (SGA) births among a cohort of female veterinarians in relation to selected occupational factors, including clinical practice type (CPT).

Design—Retrospective cohort survey.

Sample Population—2,997 female graduates from US veterinary colleges between 1970 and 1980.

Procedure—Relevant health and occupational data were collected through a self-administered mail questionnaire with telephone follow-up of nonrespondents. Absolute and relative risks of PTD and SGA births were estimated in relation to maternal CPT at the time of conception and exposure to 13 occupational factors. Attempts were made to control confounding by use of multiple logistic regression analyses.

Results—Absolute and relative risks of PTD were highest for veterinarians employed in exclusively equine clinical practice. Although several increased, none of the CPT-specific relative risk estimates were significantly different from the null value of 1. Exposure-specific analyses indicated that occupational involvement with solvents among exclusively small animal practitioners was associated with the highest relative risk of PTD. A small number of SGA births limited information that could be obtained from these analyses. Overall absolute risks of PTD and SGA births among cohort members were much lower in comparison with the general female population.

Clinical Implications—Given the large number of women currently practicing and entering the profession of veterinary medicine, clinical tasks associated with potential reproductive hazards should be approached with heightened awareness and increased caution, especially activities that may involve exposure to solvents. (*J Am Vet Med Assoc* 1998;213:61–67)

The practice of veterinary medicine is associated with a wide variety of occupational health concerns, such as zoonotic diseases, cancer, reproductive disorders, job-related stress, and considerable physical demands.[1-6] The potential for adverse health effects from occupational exposures in clinical practice is of concern to members of the veterinary profession, especially female veterinarians of childbearing age.

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Supported in part by grant No. R03 OH02380 from the National Institute for Occupational Safety and Health.

The authors thank Drs. Mel Moeschberger and David Savitz, the staff of The Ohio State University School of Public Health's Biometrics Laboratory, and Mrs. Patricia Price for assistance.

Interest in the risk of adverse reproductive outcomes among female veterinarians is fairly recent and reflected in a small number of completed or continuing studies.[7-9] Although results of research conducted thus far have indicated that female veterinarians (or at least certain subgroups of female veterinarians) may be at greater risk of adverse pregnancy outcomes, such as spontaneous abortion,[8] the epidemiologic associations identified have been weak. Furthermore, these investigations have suffered from several limitations, including small populations, potential misclassification of occupation,[10] and low survey response rates.[9] There are inherent difficulties in conducting epidemiologic studies of female veterinarians because they are relatively few in number, are geographically dispersed, cohort effects may be encountered,[11] and the "healthy worker effect"[12,13] may complicate analyses and confound results. On the other hand, female veterinarians are a relatively homogeneous group in terms of race and socioeconomic status, and as highly educated health professionals, high survey response rates and high-quality responses would be expected.

Given the variety of workplace hazards that veterinarians may encounter,[1-3] epidemiologic studies of potential adverse health outcomes associated with such exposures are warranted, especially when these studies focus on female veterinarians of childbearing age. Motivated by concern about possible adverse effects of occupational exposures on pregnancy outcomes, we analyzed data from a survey of female veterinarians that pertained to **preterm delivery (PTD)** and **small-for-gestational-age (SGA)** births. Although analyses consisted primarily of comparing different subgroups of the cohort, we also considered risks of PTD and SGA births among veterinarians in relation to the general population.

Materials and Methods

Population—Female veterinarians who graduated from US veterinary colleges between 1970 and 1980 (inclusive) were selected for participation in the study (n = 2,997). As previously described,[8] cohort identification relied primarily on membership records of the AVMA and on annual graduation rosters of each veterinary college. Agreement between the 2 lists was high, because more than 93% of female graduates were AVMA members. Assistance in cohort ascertainment and identification was also sought from veterinary college alumni associations and state veterinary organizations.

Questionnaire—The questionnaire was designed to be self-administered and was distributed by mail. Personal interviews with practicing veterinarians and testing of the questionnaire were conducted prior to distribution. Information on the following variables was collected: chronic illness, hospitalizations, unintentional occupational injuries, reproductive history, zoonoses, preexposure rabies prophylaxis and rabies exposure, employment history, tobacco, alcohol, and illicit drug use, and radiation film badge use. Questions addressing reproductive health and pregnancy were modeled after the National Center for Health Statistics' 1980 National Natality Survey.[14] Type of veterinary practice was characterized with codes developed by the AVMA (eg, type of professional activity, employer type, and employment function). Mean time for completion of the questionnaire was 35 minutes.

Implementation—A slightly modified version of Dillman's total design method for mailed, self-administered questionnaires was used.[15] A letter of explanation accompanied the questionnaire in the first mailing (January 1987). One week later, a personalized postcard reminder was sent thanking participants and encouraging all others to complete the questionnaire as soon as possible. Two additional mailings of the questionnaire were conducted, with the last mailing 7 weeks after the first. All mailings were accompanied by a cover letter, telephone numbers of the investigators, and a stamped, addressed return envelope.

To maximize response rate, telephone follow-up of all nonrespondents was conducted. Complete survey information was again requested by telephone or mail. In an attempt to assess nonresponse bias, an abridged version of the questionnaire was offered to those refusing to answer all questions. The telephone follow-up phase of the survey was conducted February through May 1988.

Outcomes—The unit of analysis for this study was an individual pregnancy. Pregnancies included in analyses were restricted to those that began after graduation from veterinary college and for which the veterinarian reported only 1 job at time of conception. This last restriction was applied because including pregnancies associated with multiple jobs would have combined the effects of mixed exposures with those of heterogeneous clinical practice type (CPT) for the same woman.

Two pregnancy end points were considered in analyses described here: PTD (all singleton live born infants delivered before completion of 37 weeks of gestation) and SGA (all singleton live born infants whose gestational age and weight placed them in the lowest 10th percentile, compared with gender- and parity-specific norms) births.[16] Infants of gestational ages outside the tabulated range (< 21 or > 44 weeks) were omitted from analyses.

Low birth weight was not examined as an end point for its association with occupational factors. Alberman[17] emphasized the need to further define this outcome by classifying infants as low birth weight only after allowing for gestational age, sex, birth order, and maternal height and weight characteristics. It is recognized that mechanisms by which infants are born too early could be entirely distinct from factors that limit their size.[18,19]

Exposures—Self-reported occupational exposures to specific agents and CPT at time of conception were the 2 types of exposure variables considered. An occupational exposure history was requested in the employment history section of the questionnaire. In this section, respondents gave categorical responses (yes, no, or don't know) to questions addressing 13 occupational exposures. A priori selection of exposures was guided by literature reports of potential reproductive hazards and by the judgment of the investigators. Exposure was defined as job-related exposure associated with employment after graduation from veterinary college, and duration of exposure was determined by the beginning and ending years for each job. If exposure was reported, it was assumed that this exposure was present throughout the time the job was held. Consistent with our study of spontaneous abortion risks among female veterinarians,[8] a pregnancy was classified as "exposed" if the year of conception coincided with the job-specific years of employment for which exposure was reported. For CPT, 2 reference groups were created to permit the comparison: "in" and "not in" veterinary clinical practice. The first reference group was defined as all female veterinarians employed at the time of conception in a job other than veterinary clinical practice. Because the effect of employment status on adverse reproductive outcome is uncertain, a second reference group was defined as all female veterinarians not in veterinary clinical practice at the time of conception (thus including a small number of unemployed women).

Confounders—For both pregnancy outcomes, several nonoccupational risk factors (ie, covariates) were considered potential confounders. Selection of covariates was guided by empirical evidence and theoretical considerations. Nonoccupational risk factors for adverse pregnancy outcomes were initially identified through a comprehensive literature review.[20-23] Potential confounders included in multivariate statistical models were maternal age, maternal height, gravidity, prior alcohol and tobacco use (as reported in the questionnaire), history of spontaneous abortion, history of low birth weight birth, history of PTD, and history of births of infants having congenital anomalies.

Statistical methods—Both types of exposure variables were examined separately in relation to each pregnancy outcome by use of a multiple logistic regression procedure contained in a software package designed for analysis of clustered or correlated data.[24] The logistic model is appropriate for historical cohort designs,[25] and this software permitted us to take into account the potential autocorrelation created by multiple pregnancies in a single woman. Logistic regression analysis has been widely used to examine exposure data in relation to adverse reproductive outcomes, such as spontaneous abortion,[26] fetal loss,[27] and congenital malformations.[28]

Results

Response to survey—The previously described procedures resulted in contact with 2,807 (93.7%) cohort members. Of the remaining 190 members, 171 were untraceable and 19 had died. In response to the first mailing, 2,427 completed questionnaires were received. Telephone contacts yielded an additional 105 completed questionnaires. Therefore, the overall response rate among those contacted was 90.2% (2,532/2,807). Responses to the abridged questionnaire were too limited to be informative (n = 18).

Respondents were born between 1933 and 1958, and most (89.4%) were born during the decennium from 1946 to 1955. Mean age of respondents was 36.1 years in 1987 (year questionnaire was distributed), and 85% of respondents were less than 40 years old. Nearly all respondents were Caucasian (2,435; 96.2%), which reflected the racial composition of US veterinary students in the 1970s.

Pregnancy experience of cohort—Affirmative answers to the question "Are you now or have you ever been pregnant?" were received from 1,444 (57%) respondents. When asked how many times they had been pregnant, 50.4% reported 1 to 3 pregnancies. Mean number of pregnancies per respondent was 1.2 (median, 1). Among the subgroup of respondents reporting at least 1 pregnancy, mean number of pregnancies was 2.1 (median, 2). Of this subgroup, 88.5% reported no more than 3 pregnancies. Approximately

Table 1—Pregnancy outcomes among a cohort of female veterinarians reporting one or more pregnancies

Outcome	All pregnancies No.	All pregnancies %	Postgraduation pregnancies only No.	Postgraduation pregnancies only %
Live birth delivery	2,038	65.8	1,828	73.4
Twin birth	29	0.9	27	1.1
Singleton birth	2,009	64.8	1,801	72.4
Low birth weight*	72	[3.6]	62	[3.4]
Small for gestational age*	37	[1.8]	27	[1.5]
Preterm delivery*	107	[5.3]	96	[5.3]
Congenital anomaly*	98	[4.9]	89	[4.9]
Elective abortion	562	18.1	241	9.7
Fetal death	344	11.1	280	11.2
Early	324	10.5	264	10.6
Late	20	0.6	16	0.6
Pregnant at time of survey	114	3.7	114	4.6
Ectopic/tubal pregnancy	22	0.7	16	0.6
Not stated	18	0.6	10	0.4
Total	3,098	100.0	2,489	99.9

*Percentage shown in square brackets based on total No. of singleton live births. Notice that the outcome categories low birth weight, small for gestational age, preterm delivery, and congenital anomaly are not mutually exclusive.

27,000 postgraduation person years were contributed by the 2,532 respondents.

Pregnancy outcomes—Survey respondents reported 3,098 pregnancies (Table 1). Most (65.8%) pregnancies resulted in live birth deliveries; nearly all of these were singleton births. Among 2,009 singleton births, 72 (3.6%) were classified as low birth weight infants (< 2,500 g), 107 (5.3%) as PTD (< 37 completed weeks of gestation), 37 (1.8%) as SGA, and 98 (4.9%) were reported to have at least 1 congenital anomaly. Only 16 singletons born at term were classified as low birth weight. Among 344 fetal deaths, 324 were classified as early fetal deaths (ie, spontaneous abortion [fetal loss prior to 20 completed weeks of gestation]), indicating an overall miscarriage risk of 0.105 (324/3,098).

To link occupational exposure data to PTD and SGA births, it was necessary to restrict analyses to pregnancies for which conception occurred after graduation from veterinary college (when employment and exposure histories began). There were 2,489 pregnancies reported as beginning after graduation, and 1,828 (73.4%) resulted in live birth deliveries (Table 1). There were 1,801 singleton live births, of which 62 (3.4%) were classified as low birth weight, 96 (5.3%) as PTD, 27 (1.5%) as SGA, and 89 (4.9%) were described as having at least 1 congenital anomaly. Of 62 singleton low birth weight infants, 12 were delivered at term. Fetal deaths (n = 280) were the result of 11.2% of these pregnancies, and 264 (94.2%) of these deaths were classified as spontaneous abortions.

PTD—Absolute risk of PTD varied widely across CPT, from a low of 0.046 for women who were not in clinical practice to a high of 0.143 for women in practices that were exclusively equine. Overall risk of PTD for women employed in any type of veterinary clinical practice was 0.059, which is lower than that of the general population by a factor of 2.[26] However, the number of PTD and postgraduation singleton live births varied considerably by practice type (Table 2).

Estimated relative risks of PTD also varied widely, ranging from 0.9 among cohort members employed in mixed practices at conception to 3.5 among members employed in practices that were exclusively equine (Table 2). Although the slightly high relative risks for women in large animal practices and the notably high relative risk of 3.3 for women in practices that were exclusively equine draw attention to the possible influence of CPT, the tabulated relative risks of PTD for women in the several clinical practice subgroups were not significantly different from the null value of 1. Use of different reference groups had little impact on the results of our study, although it appears that there may be a small, protective effect associated with unemployment. Multivariate adjustment, using logistic regression for nonoccupational confounders, had little effect on the magnitude of crude relative risks (ie, strong confounding appeared to be absent).

Exposure data indicate that pregnant female veterinarians have occupational involvement with a wide

Table 2—Absolute and relative risks of preterm delivery (PTD) among a cohort of female veterinarians by clinical practice type (CPT) at time of conception*

CPT at conception	No. of PTD	No. of singleton live births	Crude PTD risk	Model 1† cRR	Model 1† aRR§	Model 1† 95% CI‖	Model 2‡ cRR	Model 2‡ aRR§	Model 2‡ 95% CI‖
Exclusively small animal	52	862	0.060	1.1	0.9	0.4–2.4	1.3	1.2	0.5–2.8
Mixed animal¶	25	463	0.054	0.9	0.9	0.3–2.5	1.2	1.2	0.5–3.0
Exclusively large animal	5	56	0.089	1.6	1.5	0.4–5.7	2.0	1.7	0.4–6.6
All equine	3	21	0.143	2.7	2.9	0.6–15.2	3.5	3.3	0.6–18.1
Employed in any type of clinical practice	82	1,381	0.059	1.0	1.0	0.4–2.6	1.3	1.3	0.5–3.0
Employed but not in clinical practice#	7	121	0.058	1.0	1.0	NA	NA	NA	NA
Not in clinical practice**	8	174	0.046	NA	NA	NA	1.0	1.0	NA

*Preterm delivery defined as all singleton live born infants delivered before 37 completed weeks of gestation. Analyses restricted to women reporting only 1 CPT at the time of conception. †Reference group for model 1: employed but not in clinical practice. ‡Reference group for model 2: not in clinical practice. §Logistic regression was used to adjust for woman's height, maternal age, gravidity, cigarette smoking status, alcohol consumption status, presence of any birth defect (index pregnancy), history of low birth weight birth, and history of spontaneous abortion. ‖Model-based 95% confidence interval (CI) around aRR. ¶Clinical practice with any combination of small and large animal patients. #Reference group for model 1. **Reference group for model 2 (includes employed and unemployed veterinarians).

cRR = crude relative risk; aRR = adjusted relative risk; NA = not applicable.

Table 3—Agent-specific absolute and relative risks of PTD among a cohort of female veterinarians

Occupational exposure	No. of singleton live births: Exposed	No. of singleton live births: Not exposed	Crude PTD risk among live births: Exposed	Crude PTD risk among live births: Not exposed	aRR*	95% CI†
Disinfectants	1,398	88	0.060	0.046	1.2	0.3–4.4
Antibiotics	1,347	135	0.060	0.044	1.3	0.5–3.6
Insecticides	1,338	143	0.061	0.042	1.3	0.5–3.6
Formaldehyde	1,294	187	0.061	0.048	1.2	0.6–2.7
Non-DES hormones	1,172	302	0.056	0.066	0.9	0.5–1.6
Solvents	1,046	329	0.063	0.049	1.4	0.7–2.6
Radiation	1,017	413	0.052	0.080	0.6	0.4–0.9
DES	1,023	451	0.052	0.073	0.7	0.4–1.2
Nonhalothane anesthetics	1,020	452	0.063	0.049	1.3	0.8–2.2
Halothane	813	661	0.057	0.062	0.9	0.5–1.4
Antineoplastics	542	906	0.061	0.056	1.1	0.7–1.7
Heavy metals	248	930	0.065	0.058	1.1	0.6–2.0
Ethylene oxide	224	1,101	0.067	0.055	1.1	0.6–2.1

*Logistic regression was used to adjust for woman's height, maternal age, cigarette smoking status, alcohol consumption status, gravidity, history of birth defects, history of low birth weight birth, and history of spontaneous abortion.
†Model-based 95% confidence interval (CI) around aRR.
aRR = adjusted relative risk; DES = diethylstilbestrol.

Table 4—Agent-specific absolute and relative risks of PTD among a cohort of female veterinarians in exclusively small animal practice

Occupational exposure	No. of singleton live births: Exposed	No. of singleton live births: Not exposed	Crude PTD risk among live births: Exposed	Crude PTD risk among live births: Not exposed	aRR*	95% CI†
Disinfectants	813	3	0.062	0	NA	NA
Antibiotics	797	19	0.060	0.105	0.5	0.1–2.7
Insecticides	796	18	0.063	0	NA	NA
Formaldehyde	749	65	0.061	0.062	1.0	0.4–2.8
Non-DES hormones	702	110	0.057	0.082	0.8	0.3–1.7
Solvents	585	155	0.067	0.032	2.6	1.0–6.6
Radiation	620	158	0.050	0.114	0.4	0.2–0.7
DES	670	142	0.057	0.084	0.7	0.3–1.6
Nonhalothane anesthetics	641	167	0.066	0.042	1.6	0.7–3.6
Halothane	538	271	0.050	0.085	0.5	0.3–1.0
Antineoplastics	381	416	0.060	0.063	1.0	0.6–1.9
Heavy metals	136	488	0.052	0.066	0.8	0.3–1.9
Ethylene oxide	141	585	0.064	0.055	1.3	0.6–2.9

NA = not applicable.
See Table 3 for key.

range of hazards. Adjusted relative risk estimates for PTD for each of the 13 occupational exposures (Table 3) ranged from 0.6 (radiation) to 1.4 (solvents), with most close to the null value of 1. Radiation appears to have a prima facie, but likely spurious, protective effect.

When analyses were restricted to pregnancies of veterinarians employed in practices that were exclusively small animal (Table 4), similar results were obtained with 1 notable exception: solvents (adjusted relative risk, 2.6). Although adjusted relative risks for radiation (0.4) and halothane (0.5) are less than 1, both estimates probably represent spurious findings.

SGA births—As for PTD, absolute and relative risks of SGA birth varied by CPT. The number of postgraduation pregnancies classified as SGA was quite small (n = 27) and did not permit calculation of agent-specific risks or multivariate adjustment for potential confounders. Overall risk of SGA among cohort members was 0.015 (Table 1).

Discussion

Results of our study failed to indicate any strong associations between occupational factors and PTD and SGA births among a cohort of female veterinarians. However, an increased risk of PTD was evident among large animal practitioners, and a significant association was found between occupational exposure to solvents and risk of PTD among small animal practitioners. Wiggins et al[6] found higher rates of trauma among large animal practitioners, which may reflect the greater physical demands of this type of clinical practice. Although evidence linking physical demands during pregnancy with PTD and other adverse outcomes appears weak and inconsistent,[29] Mamelle et al[30] did find an association between the rate of premature births and an occupational fatigue index. In separate analyses,[e] we did not find an association between risk of PTD and the number of hours worked per week, which was an important factor in the study by Mamelle et al.[30] Whereas the strenuous physical demands of large animal practices invite speculation as to its role in PTD, results of studies focusing on postural fatigue and lifting refute such a hypothesis. With respect to the role of solvents in PTD, a recently published review[31] refers only to a study by Lipscomb et al.[32] Results of this population-based, cross-sectional study of more than 1,000 pregnant women indicated a weak, nonsignificant association between self-reported occupational exposure to solvents and premature birth (confounder-adjusted relative risk estimate, 1.90; 95% confidence interval, 0.30 to 3.99). Prior evidence linking occupational solvent exposure with PTD is, therefore, sparse, and limitations of the study design must be considered when evaluating the reliability of the association in this study.

Determination of pregnancy outcomes in the study reported here relied on self-reported responses of cohort members. Self-reported data are subject to recall errors. Joffe[33] considered methodological issues arising from use of retrospective questionnaire-based surveys to study reproductive effects of occupational exposures and concluded that reservations concerning the validity of such data have been overemphasized. He found recall regarding birth weight and gestational age to be accurate for 20 years or more. Although there is no reason to believe that live births were reported inaccurately by participating veterinarians, it is possible that adverse outcomes may not have been reported because of failure to recall or misreporting of past events. For example, faulty memory may have affected reporting duration of gestation, especially because information was not obtained that would have more accurately indicated the onset of pregnancy (eg, date of the last menstrual period). Poor recall may also have affected the accuracy of reported birth weights of live born infants unless the respondent made use of records of past births that contained this information.

Because a single national standard for assessing intrauterine growth retardation is not available, the nomogram published by Brenner et al[16] was chosen as the basis for classification of infants born to female veterinarians as SGA. Limited overlap of preterm and SGA infants (1% of preterm infants were SGA and 5% of SGA infants were preterm) indicated that separation of prematurity from size was effective. Savitz et al[34] obtained comparable results when using this nomogram. The price of this refinement in study design was a loss of statistical power, because although there were 62 low birth weight postgraduation pregnancies available for outcome analyses, only 27 live births (1.5% of singleton live births) could be classified as SGA on the basis of the nomogram.

Given the weak associations found in this study, variation in risk is likely best explained by factors other than occupational exposure to chemical, physical, and biological agents. Although the magnitude of covariate-adjusted relative risk estimates indicates little, if any, uncontrolled confounding by known risk factors, it is possible that other important risk factors for adverse pregnancy outcome were not addressed by this survey. In particular, caffeine consumption among female veterinarians was not assessed. Caffeine consumption during pregnancy has been evaluated for its association with adverse pregnancy outcomes with contradictory results: caffeine consumption has been linked with increased risk of prematurity by several investigators,[35-40] whereas no association has been reported by others.[41-44] Pastore and Savitz[45] concluded that their "results provide evidence against an adverse effect of caffeine intake on preterm delivery." Smoking also has been identified as an important confounder in studies of the relationship between caffeine use and risk of low birth weight.[36] Furthermore, among risk factors considered in the present study, maternal cigarette smoking and alcohol consumption could not be temporally linked with each gestation (ie, questions about smoking and drinking were not posed for each pregnancy). It is possible that women who reported histories of moderate to heavy use of alcohol or tobacco might have decreased or eliminated those behaviors during pregnancy.

Other risk factors, such as job-related physical stress and history of prior elective abortion, were also evaluated but with little success. The number of reported hours worked per week could only serve as a proxy measure for physical stress encountered in a particular job. Inclusion of this variable as a covariate in the multivariate analyses did not improve the explanatory power of the models, although greater risk of PTD among large animal practitioners invites speculation that physical exertion associated with this CPT may be involved. Effects of elective abortion on pregnancy outcome were also examined, but our attempts to include this as a covariate in the models were unsuccessful because of its limited dispersion.

Previous studies[13] of occupational exposures and pregnancy outcome have used pregnancies of unemployed women, employed and unexposed women, or a combination of both as comparison groups to women exposed to occupational hazards during pregnancy. It has been suggested that women who maintain employment while pregnant are an inherently more fit subpopulation of all pregnant women.[12,46] Other investigators have suggested that the reverse is true; that is, women who have had an unfavorable pregnancy outcome are more likely to stay in the workforce or to return to work more quickly after pregnancy.[13,46-48] Because CPT analyses were motivated by concern regarding the potentially hazardous nature of clinical practice, the fundamental contrast was whether the woman was "in" or "not in" veterinary clinical practice. Ambiguity surrounding the question of the most appropriate reference group (with respect to employment status) prompted us to conduct 2 separate analyses (Table 2).

Similarly, agent-specific analyses used a combination of pregnancies during which women were employed or not employed as the reference group ("employed" pregnancies were also "unexposed" pregnancies). Although it would have been preferable to use only pregnancies during which women were employed and unexposed as the reference group, most pregnancies began while women were working in jobs where exposures were reported to have occurred. Therefore, including only these pregnancies during which women were employed and unexposed would have resulted in insufficient numbers for meaningful statistical analyses. We acknowledge that an employed pregnant woman included in the reference group for any agent-specific analysis could also be classified as an exposed pregnant woman in other agent-specific analyses. In this sense, there were no unexposed employed pregnant women among the veterinarians surveyed, given the extent of reported occupational exposure to various agents.

Use of pregnancy as the unit of analysis has been recognized as a source of bias caused by the nonindependence of pregnancies contributed by the same woman. Problems caused by this autocorrelation arise primarily from 2 sources: heterogeneity of risk and control of fertility.[49] In previous epidemiologic studies of adverse pregnancy outcomes, several approaches have been taken, including restriction of analyses to first pregnancies only or to randomly selected pregnancies. In the present study, sample size considerations prevented reduction of the number of outcome events, although when analyses that used CPT as a proxy measure of exposure were repeated to include first pregnancies only, differences in absolute risks, relative risks, and 95% confidence intervals across CPT categories, compared with results of calculations that included all pregnancies, were negligible. Attempts to control for potential bias resulting from the "mother effect" produced essentially the same results and supported the same conclusions.[24]

Although respondents contributed nearly 2,500 postgraduation pregnancies for analyses, the number was small enough that it affected the statistical power of the study, degree of variable refinement, and precision of relative risk estimates. Sparseness of data created problems in formation of comparison categories for exposure and pregnancy outcomes. For example, use of CPT as a proxy exposure variable required that several specific practice types be combined to form categories (eg, exclusively small animal, mixed, exclusively large animal) that were large enough to produce meaningful results. Associations may have been missed because of our inability to consider all individual practice types.

Post hoc power calculations for agent-specific findings (Table 3; based on detection of a minimum relative risk of 2.0 for $\alpha = 0.05$) yielded estimates of 80% or more for 9 of 13 exposures. With respect to agent-specific findings for practitioners in small animal practice (Table 4), only 3 of 13 power estimates for exposures were 80% or more. All post hoc power calculations for CPT comparisons (Table 2) produced values that were less than 50%. Therefore, negative results of this study may, in part, be explained by low statistical power.

It should be emphasized that the overall risk of PTD of 0.053 (Table 1) for female veterinarians compares favorably with data indicating an absolute risk of PTD of 0.110 for the general population of US women.[50] For US Caucasian females, a subgroup of the population that is racially similar to the cohort examined in the present study, overall risk of PTD was 0.095. The beneficial role of high social class and education was demonstrated by Querac[51]: among white females with at least 16 years of education, PTD occurred in only 5.4% of live births. This value is virtually identical to that obtained in our study.

Comparison rates for SGA births are difficult to obtain because population-based sources tend not to categorize births in this way. Therefore, we were not able to compare our observed risk of SGA births among female veterinarians to that of a similar population. An approximation can be made by considering full-term low birth weight births, a category that includes most growth retarded infants. Using this estimate, intrauterine growth retardation was determined to be a problem for 2.3% of full-term live births to US white females in 1985.[52] Although a breakdown by level of maternal education was not provided, this estimate is more than twice that observed among members of our cohort.

In conclusion, it should be seen as reassuring that no strong associations between occupational factors and PTD and SGA births were found in our study. However, because an increasing number of women have been entering veterinary medicine, our findings indicate that clinical tasks involving potential reproductive hazards should be approached with heightened awareness and increased caution, especially activities that may involve exposure to solvents.

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