# Relationships between demographic variables and lead toxicosis in cattle evaluated at North American veterinary teaching hospitals

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**Objective**—To determine associations between age, sex, breed, and month and year of admission and the diagnosis of lead toxicosis in cattle.

**Design**—Retrospective case-control study.

**Sample Population**—Records of all cattle evaluated at North American veterinary teaching hospitals during the years 1963 to 2002, which were available through the Veterinary Medical Database.

**Procedures**—Logistic regression was used to evaluate the associations between postulated risk factors and the occurrence of lead toxicosis in cattle and predict the occurrence of the diagnosis of lead toxicosis in cattle.

**Results**—413 cases of lead intoxication and 202,363 control cattle were identified and met the inclusion criteria. Cattle < 4 years of age were at increased risk for the diagnosis of lead intoxication relative to cattle ≥ 4 years of age. Cattle ≥ 2 months and < 6 months of age had the greatest risk for lead intoxication (odds ratio, 12.3). Angus cattle were at greater risk for toxicosis (odds ratio, 1.95), compared with other breeds. The risk of lead toxicosis was greater before 1985 (odds ratio, 1.94) than the risk thereafter. The risk of lead toxicosis diagnosis was greatest in the months of May, June, July, and August.

**Conclusions and Clinical Relevance**—Lead toxicosis in cattle was associated with age < 4 years and the Angus breed. A seasonal pattern existed with peak occurrence in the late spring and summer. The occurrence of lead toxicosis has declined over time. (*J Am Vet Med Assoc* 2008;233:955–959)



Lead is the most common metal toxin of cattle.[1–3] Lead poisoning is 10 times as common in cattle as in any other domestic animal species.[4] The most common form of lead toxicosis is the acute syndrome that occurs following ingestion of large quantities of lead in a short period.[5,6] This form has been associated with the indiscriminate eating habits of cattle.[1,2,5,7,8] The greatest number of toxicoses has been recorded in the summer[2] and spring.[3,5] Younger cattle are reported to be predisposed to lead toxicosis because they absorb a larger proportion of ingested lead, compared with older cattle.[9] Milk-based diets and, in particular, lactose-containing diets appear to promote the absorption of lead. Poisoned cattle have been reported to shed lead in their milk, providing an additional source of lead in nursing calves.[10] In 1 report, > 50% of cattle lead toxicoses occurred in cattle < 6 months of age.[8]

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Multiple sources of lead have been identified.[2,5,7] Batteries, lead-containing paints, motor oil, linoleum, fumes and dust from lead smelters, putty cans, and forages contaminated with industrial fumes[11] are some of the common sources. Nervous system signs predominate in acutely affected cattle and generally appear within 12 to 24 hours after lead ingestion.[2,12] Observed clinical signs are suggestive of a symmetric, diffuse, cortical disease. These clinical signs include signs of depression, cortical blindness, hyperesthesia, teeth grinding, muscle tremors, and gait abnormalities.[5] The presumptive diagnosis of lead toxicosis is based on a history of exposure and the clinical signs. Although no single test result accurately defines lead content in the body,[5] blood lead concentrations exceeding 0.3 ppm are considered diagnostic for acute lead toxicosis.[12] Without treatment, acute lead toxicosis fatality rates approach 100%.[13] Case fatality rates may be reduced to < 50% with treatment.[13] Treatment typically is based on the administration of calcium disodium EDTA and thiamine.[12–17]

Age, breed, and seasonal effects on lead toxicosis have been examined[1,3,5,18]; however, the association between sex and lead toxicosis has not been examined, to our knowledge. Additionally, the relatively small case population of preceding studies and limited data availability precluded the use of multivariate approaches that would have controlled the potential for spurious relationships caused by confounding. These multivari-

ate approaches are particularly important because we anticipated that seasonal calving patterns had the potential to create confounding relationships among age, month of admission, and the diagnosis of lead toxicosis. Therefore, the purpose of the study reported here was to identify risk factors for the diagnosis of lead toxicosis in cattle. Changes in occurrence of lead toxicosis over time also were examined.

## Materials and Methods

**Source of clinical records**—Records of all cattle evaluated at North American veterinary teaching hospitals from 1963 to 2002 available through the Veterinary Medical Database were accessed. Cattle with the diagnosis of lead toxicosis recorded in the database were defined as cases. During this time interval, records were submitted to the database from 27 North American veterinary teaching hospitals. The control group was defined as all cattle without the diagnosis of lead toxicosis. Initially, a statistical software[a] package was used to sort data with regard to risk factor categories and delete records on the basis of defined exclusionary criteria. Exclusionary criteria were applied equally to case and control records. Records with missing data for age, sex, breed, and month or year of admission were deleted from the data set. The data set was limited to cattle of the female, male sexually intact, and male castrated sexes. Records for which sex was identified as unknown or age was < 2 weeks were deleted. Records of all cattle of either bison or water buffalo ancestry were deleted. Each case and control individual was represented only once in the final working data set. When multiple records for 1 animal were available, only the last record from that individual was retained. The number of case and control clinical accessions deleted by application of the exclusionary criteria and deletion of duplicate entries were determined and reported.

**Statistical analysis**—Logistic regression models were developed that predicted the probability of the diagnosis of lead toxicosis as a function of postulated risk factors with the assistance of a statistical software package.[b] Risk factors for the occurrence of lead toxicosis that were considered included age, sex, breed or breed group, month of hospital admission, and year of hospital admission. Age groups were defined in a manner consistent with categories defined by the Veterinary Medical Database, and strata with low numbers of observations were combined, resulting in the following age categories: ≥ 2 weeks and < 2 months, ≥ 2 months and < 6 months, ≥ 6 months and < 1 year, ≥ 1 year and < 2 years, ≥ 2 years and < 4 years, and ≥ 4 years. Sexes considered included sexually intact female, sexually intact male, and castrated male. Dairy usage was assigned to all cattle of the Holstein, Guernsey, Jersey, Milking Shorthorn, Brown Swiss, Ayrshire, and mixed dairy breeds. All other cattle were classified as beef cattle. Breeds for which the diagnosis of lead toxicosis was reported at least 10 times were assigned a specific breed group. All other breeds were combined into either a dairy (other breed) or beef (other breed) group. As a consequence, breed groups considered included Angus, Charolais, Hereford, Holstein, Jersey, Shorthorn, beef (other breed), and dairy (other breed). Month of hospital admission was defined on the basis of calendar month. Year of admission was represented by a binomial variable that arbitrarily divided the 38 years represented in the data set into 2 roughly equal halves, prior to 1985 and 1985 to 2002. The risk of lead toxicosis was calculated relative to baseline exposure concentrations that included the male castrated sex, age > 4 years, the dairy other breed category, during or after 1985, and the month of December.

The analytic method considered all variables simultaneously and included those variables in the model for which at least 1 level of a variable was significantly ($P < 0.10$) associated with the diagnosis of lead toxicosis. When any level of a variable was deemed significant, all levels of the variable, regardless of significance, were included in the model. Models that considered second-order interactions also were constructed. Models were evaluated for goodness-of-fit by use of the Pearson $\chi^2$ statistic, and the model with the highest ratio of the $\chi^2$ statistic divided by the *df* was deemed to have superior descriptive value.[19] Models for which the software package identified a convergence issue were rejected. Ninety-five percent confidence intervals were calculated for the regression coefficient for each level of each variable included in the model. Confidence intervals that were mutually exclusive were considered indicative of differing risk of lead toxicosis. Regression coefficients were used to calculate the odds ratio for each level, estimating the risk of the diagnosis of lead toxicosis relative to the defined baseline exposure.[20] Significance was defined as $P < 0.05$.

## Results

A total of 427 accessions with the diagnosis of lead toxicosis were identified in the Veterinary Medical Database. Of the 427 accessions, 9 (2.11%) were removed from the data set by use of the previously defined exclusionary criteria. An additional 5 of 427 (1.17%) accessions were followed by a second accession identified by the same individual; hence, these records were removed from data set by use of the previously defined strategies. A total of 255,060 control accessions were originally identified. Of these controls, 5,346 (2.10%) were removed by use of the exclusionary criteria and an additional 47,333 (18.56%) accessions were removed because they constituted earlier accessions identified by the same individual. The final data set included 202,776 accessions, of which 413 had a diagnosis of lead toxicosis and the remainder were control cattle.

Prior to 1985, the database included 317 cattle with lead toxicosis and 126,926 control cattle. From 1985 to 2002, the database included 96 cattle with lead toxicosis and 75,437 control cattle. Lead toxicosis was diagnosed in 252 female cattle, 106 bulls, and 55 steers. The 202,363 control cattle included 140,367 females, 52,379 bulls, and 9,617 steers. Of the 413 cases of lead toxicosis, 113 were in dairy cattle and 300 were in beef cattle. The controls included 91,441 beef cattle and 110,922 dairy cattle.

The logistic model identified that sex, age, breed group, year of admission, and month of admission were significantly associated with the diagnosis of lead toxicosis. The simple model (no interactions included; **Table 1**)

Table 1—Summary of results of a logistic regression model to predict the probability of a diagnosis of lead toxicosis in cattle evaluated at North American veterinary teaching hospitals (1963–2002) as a function of certain variables.

| Variable | Level | Coefficient (95% CI) | OR | *P* value |
|---|---|---|---|---|
| Intercept | | –8.935 (–9.822, –8.047) | | < 0.001 |
| Sex | Female | –0.155 (–0.465, 0.156) | 0.86 | 0.329 |
| | Male sexually intact | –0.681 (–1.016, –0.347) | 0.51 | < 0.001 |
| | Male castrated | * | 1.00 | * |
| Age | ≥ 2 wk and < 2 mo | 1.516 (1.042, 1.990) | 4.55 | < 0.001 |
| | ≥ 2 mo and < 6 mo | 2.508 (2.131, 2.884) | 12.28 | < 0.001 |
| | ≥ 6 mo and < 1 y | 2.233 (1.829, 2.636) | 9.33 | < 0.001 |
| | ≥ 1 y and < 2 y | 1.872 (1.495, 2.250) | 6.50 | < 0.001 |
| | ≥ 2 y and < 4 y | 0.661 (0.246, 1.076) | 1.94 | 0.002 |
| | ≥ 4 y | * | 1.00 | * |
| Breed | Angus | 0.670 (0.108, 1.232) | 1.95 | 0.020 |
| | Charolais | –0.185 (–0.895, 0.525) | 0.83 | 0.610 |
| | Hereford | 0.174 (–0.383, 0.731) | 1.19 | 0.540 |
| | Holstein | –0.286 (–0.835, 0.264) | 0.75 | 0.308 |
| | Jersey | 0.441 (–0.339, 1.222) | 1.55 | 0.268 |
| | Shorthorn | 0.135 (–0.669, 0.940) | 1.14 | 0.742 |
| | Other beef | 0.286 (–0.260, 0.831) | 1.33 | 0.305 |
| | Other dairy | * | 1.00 | * |
| Year | Prior to 1985 | 0.665 (0.430, 0.899) | 1.94 | < 0.001 |
| | During or after 1985 | * | 1.00 | * |
| Month | Jan | 0.210 (–0.562, 0.983) | 1.23 | 0.594 |
| | Feb | 0.986 (0.314, 1.657) | 2.68 | 0.004 |
| | Mar | 1.241 (0.601, 1.880) | 3.46 | < 0.001 |
| | Apr | 1.004 (0.352, 1.656) | 2.73 | 0.003 |
| | May | 1.664 (1.045, 2.282) | 5.28 | < 0.001 |
| | Jun | 1.549 (0.919, 2.179) | 4.71 | < 0.001 |
| | Jul | 1.514 (0.877, 2.151) | 4.54 | < 0.001 |
| | Aug | 1.361 (0.713, 2.009) | 3.90 | < 0.001 |
| | Sep | 0.838 (0.132, 1.544) | 2.31 | 0.020 |
| | Oct | 0.723 (0.012, 1.435) | 2.06 | 0.046 |
| | Nov | 0.202 (–0.570, 0.974) | 1.22 | 0.608 |
| | Dec | * | 1.00 | * |

*Baseline exposure strata; therefore, coefficients and *P* values are not provided, and the OR is defined as 1.
CI = Confidence interval. OR = Odds ratio.
A value of $P < 0.05$ was considered significant.

had the highest $\chi^2$-to-*df* ratio of all models considered and, as such, was deemed most descriptive of the data set. Additionally, most models that included interactions had inadequate model convergence as defined by the computer software. No interactions were significant in any of the models considered, and the number of interactions that met the inclusion criteria ($P < 0.10$) was < 5% of the interactions considered; therefore, the small number of significant interactions was deemed consistent with random events and type I error.

Bulls had a lower risk of lead toxicosis than did steers (Table 1). With regard to age, the greatest risk of lead toxicosis was in cattle from 2 months to < 6 months of age, and the lowest risk of lead toxicosis was in cattle 4 years of age or older. No significant difference was evident between cattle ≥ 6 months of age but < 1 year of age and cattle ≥ 1 year of age but < 2 years of age. Likewise, the mutually inclusive coefficient confidence intervals for cattle ≥ to 2 weeks of age and < 2 months of age and cattle ≥ 2 years of age and < 4 years of age indicated the absence of a significant difference in risk among these groups. The risk of lead toxicosis differed significantly among all other comparisons among age groups.

Only Angus cattle had an increased risk of lead toxicosis relative to the baseline exposure group, the dairy (other breed) group (Table 1). Confidence intervals of all other levels of breed were not mutually exclusive.

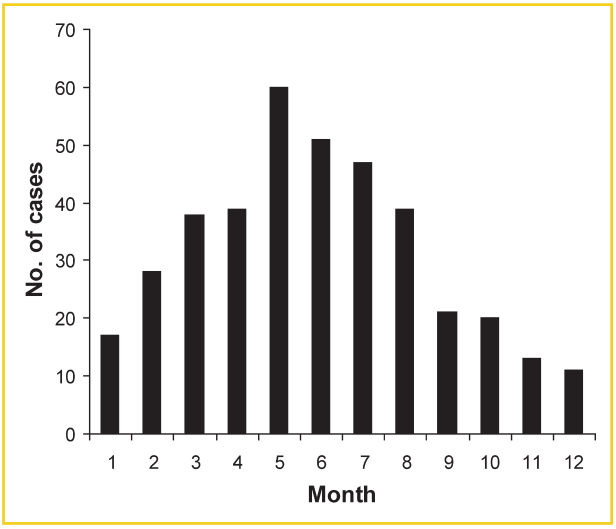


Figure 1—Distribution of lead toxicosis cases in cattle according to month of admission. Months are numbered sequentially beginning with January.

The logistic regression model revealed a highly significant temporal pattern. The risk of the diagnosis of lead toxicosis was significantly higher prior to 1985 (Table 1). There also was a seasonal pattern in the oc-

currence of lead toxicosis. Significantly increased risk relative to the baseline exposure (December) was present from February through October. The lowest risks of lead toxicosis were in the months of November, December, and January (**Figure 1**). The highest risks of lead toxicosis were in the months of May, June, July, and August.

## Discussion

The Veterinary Medical Database is maintained by a consortium of US and Canadian veterinary teaching hospitals. More than 27 institutions have contributed data. Complete records are not included in the database. Participating institutions abstract portions of records and submit those abstracts to the database. Participating institutions, unique animal identification, diagnoses, signalment, and lists of procedures performed are available through the database. Individual test results, problem lists, problems identified at evaluation, progress notes, and clinician identification are not available. Consequently, recovery of more detailed data requires the solicitation of individual records from participating institutions, and this was not performed in this study. Consequently, a study of the type reported here is dependent on the unbiased submission of accurate data to the Veterinary Medical Database from participating institutions. The basis of the diagnosis of lead toxicosis (ie, blood or tissue lead concentrations, detection of particulate lead, radiography of the gastrointestinal tract, δ-amino-levulinic acid dehydratase activity, or histopathologic lesions) was neither reported nor confirmed in this study. Furthermore, the control population may well have had undetected or undocumented exposures to lead. An additional concern regarding the Veterinary Medical Database is that the current system of anatomic location and pathologic description of diseases often does not permit differentiation of dissimilar diseases.

It is important to consider the limitations of this study and of the Veterinary Medical Database. The cattle population evaluated should be considered representative of the general cattle population. Caseload, diagnostic acumen, and accuracy of diagnosis likely vary among institutions and over time. Consequently, the present study examined the risk of the diagnosis of lead toxicosis in cattle evaluated at veterinary teaching hospitals, rather than the actual likelihood of lead toxicosis in the general cattle population. The terms occurrence or diagnosis have been used throughout the manuscript because presented data do not readily fit the definitions of either prevalence or incidence. Additionally, the control and case cattle in this study may have differed in some systematic manner, which introduced bias. The proportion of control accessions deleted because of repeated visits (18.56%) was dramatically higher than the proportion of case accessions (1.17%). Consequently, the results of this study should be interpreted with caution.

The consensus of previous reports[1,3,5,21–23] has been that young cattle are more commonly affected with lead toxicosis and that the risk of toxicosis decreases in cattle > 24 months of age. The increased susceptibility of calves has been attributed to milk-based diets that enhance the absorption of lead from the gastrointestinal tract.[24] Up to 50% of ingested lead has been reported to be absorbed in young animals.[9] Additionally, the indiscriminate feeding habits of calves[5] and the greater susceptibility of calves to lower concentrations of lead[1,24] have been hypothesized to make clinical toxicosis more likely in young animals. Although our results generally agreed with those of prior reports, our results indicated that calves < 2 months of age had a significantly lower risk than did older calves. Furthermore, cattle as old as 2 years of age should be considered highly susceptible to lead toxicosis.

Most beef calves in the United States are born in the early spring and reach the period of apparent age susceptibility during the months of apparent greatest risk: May, June, July, and August. Hence, the apparent seasonality of lead toxicosis detected in previous studies[3,5,18] could have been the result of a seasonal calving pattern that created cohorts of calves that reached the age of maximum susceptibility (2 to 6 months) coincidental with those months. The use of multivariate modeling in the present study permitted differentiation among age, breed, and month effects, which revealed a true seasonal effect during the months of maximum pasture forage availability. We hypothesize that the pattern of risk detected is consistent with pastures, rather than confinement facilities, being the predominant source of lead in cattle. Likewise, the preponderance of lead toxicoses in beef cattle supports the hypothesis that pastures are the predominant source of lead exposures. Dairy cattle are more likely to be housed in confinement than are beef cattle. No explanation is readily apparent for the increased risk of lead intoxication in Angus cattle.

The association between year of admission and risk of lead intoxication was consistent with a temporal decrease in environmental contamination. The production of leaded gasoline and the manufacture and use of lead-based paints were discontinued in the United States approximately 10 and 30 years ago, respectively.[25] In addition, most manufacturers have reduced the use of lead in the manufacturing processes of farm equipment and household goods. We hypothesize that the environmental burden posed by lead contamination and, hence, the risk of lead intoxication in cattle may have decreased over time.

a. SAS for Windows, version 9.13, SAS Institute Inc, Cary, NC.
b. PROC GEN MOD, SAS for Windows, version 9.13, SAS Institute Inc, Cary, NC.

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