Acute gastric dilatation and volvulus is a potentially catastrophic condition affecting dogs that requires immediate emergency medical and surgical treatment and intensive postoperative care to optimize the chance of a successful outcome. The reported lifetime likelihood of developing GDV is 24% in large-breed show dogs and 21.6% in giant-breed show dogs. On the basis of recent studies, the mortality rate for GDV in dogs ranges from 10% to 33%. The high incidence of GDV, together with a high mortality rate, makes GDV one of the leading causes of death for large- and giant-breed dogs. Effective preventative measures, coupled with rapid owner recognition and emergency veterinary treatment of GDV are essential to reduce the devastating impact of this condition.

Prevention relies on the identification of risk factors. To date, few risk factors for GDV have been clearly identified. The condition is assumed to be multifactorial and is influenced by dog-specific factors, management factors, environmental factors, and combinations thereof. The breed, chest conformation, body condition, genetics, age, sex, and concurrent disease state have all been identified as dog-specific risk factors. Large- or giant deep-chested purebred dogs, including German Shepherd Dogs, Great Danes, Collies, Weimaraners, Irish and Gordon Setters, Bloodhounds, Akitas, Saint Bernards, Mastiffs, Standard Poodles, Labrador and Golden Retrievers, Doberman Pinschers, and Chow Chows, are at risk for GDV. Dogs with increased thoracic depth-to-width ratio or thin or lean body condition were associated with increased GDV risk. In a major prospective cohort study in 1,637 show dogs, a history of GDV in any first-degree relative significantly increased the risk of GDV. Age was the most important risk factor for GDV in Great Danes in 1 study and was significant in several others. Male gender was found to be a risk factor in 1 study. Chronic medical conditions (e.g., inflammatory bowel disease) have also been implicated as risk factors for GDV.

Dietary management is considered a contributing factor to the development of GDV. The type of food, frequency of meals, and volume fed have all been evalu-
ated.13,15,16 Commercial dry dog food was implicated as causing GDV in 1 study.11 However, in a recent case-control study, feeding a commercial dry food did not increase the incidence of GDV.13 Feeding a single type of food was found to increase the likelihood of gastric dilatation,11 whereas the addition of table foods to a usual diet consisting primarily of dry dog food reduced the risk of acute GDV development.8 Dogs fed a larger volume of food per meal (regardless of the number of daily meals) were at a significantly increased risk of GDV, with the highest risk in dogs fed a larger volume once daily.13 In addition to single meals, small kibble (<30 mm), rapid ingestion of meals, and aerophagia have all been suggested as risk factors.18,19 Contradicting previous management recommendations for the prevention of GDV, feeding from an elevated feed bowl, moistening of dry food prior to feeding, and restricting water and exercise before and after meals were found to increase the risk of GDV in a subsequent study.10

Environmental factors may influence the risk for GDV. Interestingly, for large-breed dogs, a rural residence represented a higher risk, but for giant-breed dogs, an urban residence was associated with increased risk of GDV.10 In military working dogs in Texas, GDV was most common from November through January and least common in the hot months of June and August.17,18 This seasonal GDV variation was not detected in client-owned dogs in Switzerland, where warmer environmental temperatures were significantly associated with the occurrence of GDV.6

The interaction between a dog and its environment represents an important component of risk. Personality factors such as aggression to people and fearfulfulness or agitation in response to strangers or environmental changes were associated with an increased risk of GDV.17,19 whereas a “happy” and easygoing temperament, submission to other dogs or to people, high activity level, and attending dog shows decreased the risk of GDV.8,10 In several studies,8,10 a variety of stressful events, including kenneling and riding in the car, appeared to precipitate an acute GDV episode.

Many of the current studies evaluating risk factors for GDV in dogs have focused on unique populations of dogs (ie, show dogs and military working dogs), and most of them included relatively small numbers of dogs affected with GDV. The purpose of the study reported here was to evaluate the influence of risk factors for GDV in a large number of privately-owned dogs with GDV across a wide geographic area.

Materials and Methods

Data collection—An electronic commercial survey instrument was used to develop a questionnaire, interview dog owners worldwide, and collect the responses. The survey was initiated on June 9, 2010, and the responses entered between June 9, 2010, and August 8, 2010, were collected and analyzed.

Recruitment of survey participants—Survey participants were initially recruited by posting the electronic link to the survey on websites for dog owners (eg, www.breedingbetterdogs.com). The information was also disseminated at meetings of dog owners (eg, American Kennel Club delegates meeting) and via newsletters for dog owners and breeders (eg, American Kennel Club-Canine Health Foundation), e-mail lists for dog owners and breeders (eg, W/I search dogs and agility groups), owner-oriented dog publications (eg, Celebrating Greyhounds magazine), and e-mails forwarded by participants. Because of international access to the Internet, the survey was available to any individual in any country who had a dog, whether it had developed a GDV or not. The distribution of the survey link was not restricted or monitored; any dog owner that came across the survey could answer the questionnaire, and individuals were encouraged to share the access link with other dog owners.

Survey characteristics—The survey was anonymous and could only be completed once from any Internet protocol address. Respondents were allowed to enter data for up to 3 dogs with GDV, but were limited to entering data for only 1 dog that did not have GDV. One owner was thereby able to enter data for dogs with GDV only, dogs with GDV plus 1 dog without GDV, or only data for 1 dog without GDV. The selection of which dog’s information to enter was entirely up to the survey participant. No historical time restrictions were applied, and all breeds were eligible for inclusion. For all questions, the respondent was asked to choose 1 or more predefined answers or rate their dog on a predefined scale. In addition to the predefined choices, write-in comments were available for several questions but were not used for the analysis. The survey allowed for respondents to leave questions incomplete.

The questionnaire consisted of 3 major parts: general background information, questions applicable to dogs with GDV, and questions applicable to dogs without GDV. The general information section consisted of demographic data including the year of birth, breed, sex, neuter status and purpose (ie, family pet, performance dog, competitive sports dog, working dog, show dog) of the dog, and the country and postal code at which the dog lived. The final question in the background was a yes or no question asking whether the dog had ever had an episode of GDV requiring surgery. On the basis of the responses, the respondents were divided into 2 groups: dogs with a GDV treated with surgery (GDV group) and dogs without GDV (control group). In the GDV group, dogs that underwent surgical treatment as well as dogs that died or were euthanatized because of presumed or confirmed GDV without surgery were included. Respondents with a dog with a GDV requiring surgery were directed to a series of 44 questions organized into 4 categories. The first category of questions related to the dog-specific factors such as age at time of GDV; history of GDV in relatives; body condition score (numerical rating scale of 1 to 9); history of surgery, anesthesia, diarrhea, or other illness; speed of eating (numerical rating scale of 1 to 5); and tendency to sleep on its back. A second category of questions addressed information regarding management factors including activities of the dog (ie, dog shows, field training, schutzhund or working activities, obedience training, agility); type of diet (ie, dry kibble, canned food, raw commercial, cooked homemade, raw handmade); frequency of feeding; addition of supplements (ie, eggs, cod liver oil, fish, vitamins, cooked chicken, raw chick-
en, cheese, cottage cheese, yogurt, coat enhancer) and table foods; feeding from a raised bowl; postprandial housing (ie, kenneled, loose indoors, loose outdoors); the most relevant time (ie, immediately; 30 minutes, 1 hour, 1 to 3 hours, 3 to 6 hours, or more than 6 hours after eating) and type (ie, running outside, running inside, playing with other dogs, running the fence, jogging with owner, kenneled) of postprandial activities; lifestyle (ie, predominantly indoors, predominantly outdoors, both indoors and outdoors); routine housing (ie, loose, crate, pen); predominant company (ie, alone, other dogs, family, no family); number of hours spent with the owner each day; number of days spent with the owner each week; night time housing (ie, indoors, outdoors, or both); and company (ie, owner or handler, familiar person, unfamiliar person, alone) and location (ie, home, boarding, training facility, other familiar environment, unfamiliar environment, traveling) during the time leading up to the GDV event. The third category consisted of environmental factors, including place of residence (ie, urban, suburban, rural); presence of other dogs and cats in the household; recent addition of a new pet or person to the family; and season, outside temperature (numerical rating scale of 1 to 5, where 1 = subfreezing and 5 = extremely hot), and presence of estrus in sexually intact dogs at the time of GDV. The last set of questions referred to the dog's personality factors, such as excitable behaviors (ie, none, bats at knocks on the door, bats at strangers, bats at other dogs, is hard to control, chases tail, spins out of control, acts oblivious, runs the fence, plays with dogs), anxiety (numerical rating scale of 1 to 9) and energy level (numerical rating scale of 1 to 9). No attempt was made to obtain the information regarding surgical treatment; however, the question of whether a dog's death was related to GDV was asked. For control dogs (ie, dogs without GDV), the respondent was asked to complete 32 questions. All of the questions from the questionnaire for GDV dogs that were not directly related to the occurrence of a GDV (eg, age at the time of GDV, people in the dog's environment and location of the dog on the day of GDV, season of the year and outside temperature at the time of GDV, recent addition of a new pet or person to the household, presence of estrus in sexually intact dogs, history of recent anesthesia). These factors were not able to be compared with those of the control dogs because a comparable time period could not be established. The influence of season on the occurrence of GDV was analyzed via $\chi^2$ analysis; the rest of the data are presented as percentage of GDV dogs with the factor of interest. Because the evaluation of mortality was not an objective of the present study, the question asking whether a dog's death was related to GDV was excluded from analysis.

Results

Signalment of dogs enrolled—In the 2-month period, of the 3,557 surveys registered, 1,006 (28.3%) were excluded because they were incomplete in 1 or more of the variables that were used to build the model. The remaining 2,551 surveys were included in the analysis; the rest of the data were expressed as frequencies. Categorical data were expressed as frequencies. Logistic regression analysis was performed to evaluate risk factors for surgical GDV. Risk factors evaluated in the model included signalment, country in which the dog lived, purpose of the dog, body condition, history of surgery and other illness, cats and other dogs in the household, place of residence, diet, dietary supplements, feeding frequency, speed of eating, feeding from a raised bowl, postprandial housing, time and type of postprandial activities, energy and anxiety levels, excitable behaviors, lifestyle, routine housing, predominant company, number of hours spent with the owner or handler each day, number of days spent with the owner or handler each week, night time housing, and sleeping on the back. Univariate analysis was performed initially, and factors with a Wald test P value < 0.20 were tested in the model. Interactions between the main effects were evaluated. Factors were retained in the model on the basis of a Wald test P value < 0.05. Absence of confounding was based on a factor changing model coefficients by < 15%. The fit of the overall model was evaluated via the Pearson $\chi^2$ goodness-of-fit statistic. All analyses, including graphs to evaluate model assumptions, were performed with a commercial statistical analysis program.4

Additionally, we evaluated the responses from owners of the GDV dogs that were directly related to the occurrence of a GDV (eg, age at the time of GDV, people in the dog's environment and location of the dog on the day of GDV, season of the year and outside temperature at the time of GDV, recent addition of a new pet or person to the household, presence of estrus in sexually intact dogs, history of recent anesthesia). These factors were not able to be compared with those of the control dogs because a comparable time period could not be established. The influence of season on the occurrence of GDV was analyzed via $\chi^2$ analysis; the rest of the data are presented as percentage of GDV dogs with the factor of interest. Because the evaluation of mortality was not an objective of the present study, the question asking whether a dog's death was related to GDV was excluded from analysis.

Statistical analysis—Descriptive statistics were calculated. On the basis of non-normality of the data, continuous data were expressed as median values and ranges. Categorical data were expressed as frequencies. Logistic regression analysis was performed to evaluate risk factors for surgical GDV. Risk factors evaluated in the model included signalment, country in which the dog lived, purpose of the dog, body condition, history of surgery and other illness, cats and other dogs in the household, place of residence, diet, dietary supplements, feeding frequency, speed of eating, feeding from a raised bowl, postprandial housing, time and type of postprandial activities, energy and anxiety levels, excitable behaviors, lifestyle, routine housing, predominant company, number of hours spent with the owner or handler each day, number of days spent with the owner or handler each week, night time housing, and sleeping on the back. Univariate analysis was performed initially, and factors with a Wald test P value < 0.20 were tested in the model. Interactions between the main effects were evaluated. Factors were retained in the model on the basis of a Wald test P value < 0.05. Absence of confounding was based on a factor changing model coefficients by < 15%. The fit of the overall model was evaluated via the Pearson $\chi^2$ goodness-of-fit statistic. All analyses, including graphs to evaluate model assumptions, were performed with a commercial statistical analysis program.4

Logistic regression modeling—Because of incomplete survey data, history of GDV in relatives was unable to be included in the analysis. A question addressing history of diarrhea was excluded from further analysis as well, because of the discrepancy in the question formulation between the 2 groups.
There was a significant interaction between sex and neuter status in addition to 11 other variables with a significant association with the occurrence of a surgical GDV (Table 2). Assuming no other risk factors, the odds of GDV in sexually intact females was 0.94 (95% CI, 0.72 to 1.22), 0.83 in sexually intact males (95% CI, 0.66 to 1.05), 0.67 in neutered females (95% CI, 0.50 to 0.88), and 0.32 in neutered males (95% CI, 0.20 to 0.53). Increasing anxiety level, residing in the UK, being born in the 1990s, being a family pet, being fed dry kibble, and spending at least 5 hours a day with the owner were associated with a decreased risk of GDV (Table 2). Fish and egg dietary supplements, playing with other dogs after eating, and runs the fence after eating were associated with an increased risk of GDV (Table 2). Fish and egg dietary supplements, playing with other dogs after eating, and runs the fence after eating were associated with an increased risk of GDV (Table 2). The Pearson $\chi^2$ goodness-of-fit statistic specified good fit of the model ($\chi^2_{1}=1.299, p=0.44$).

**Group-specific information**—In the GDV group, the median age was 6 years (range, 1 to 15 years). In the 676 surveys in which the question of diarrhea in the month prior to GDV was answered, diarrhea was present in 14% of dogs. Anesthesia was performed in 12% of dogs during the 72 hours prior to the GDV. On the day of the GDV, most dogs were at home in the company of the owner or a handler, and the outside temperature was most commonly reported as the median (3) on a scale between subfreezing (1) and extremely hot (5) (Table 3). An effect of the season on the occurrence of GDV was observed ($p < 0.001$), with the smallest number of GDV cases reported during the winter and most reported GDV cases during spring (Table 3). In sexually intact dogs, 8.5% females were in season, and 16.5% of males had a bitch in season nearby during the week prior to the GDV. Only 213 responses were complete regarding new additions to the household during the 6 months prior to the GDV; however, in that group, in 160 (75%) households, a new dog was added.

The only question that was asked of the control group but not the GDV group addressed the presence of a prophylactic gastropexy. In the control group, gastropexy had been performed in 105 of 1,427 (7%) dogs.
Discussion

In this Internet-based cross-sectional survey of owners of 1,114 dogs with GDV, treated with or requiring surgery (GDV group), and 1,437 control dogs, our logistic regression analysis failed to confirm many of the previously proposed risk factors for GDV. In fact, certain activities (ie, running along the fence, playing with other dogs after meals) previously recommended to be avoided were associated with a decreased risk of GDV. Feeding dogs from a raised food bowl was strongly discouraged in a recent study but had no detectable influence on GDV in this survey.

Our study identified several new factors associated with an increase or decrease in the risk for GDV requiring surgery (Table 2). Some of the factors, however, are likely to be a result of the nature of the survey. For example, the increased risk associated with dogs living in the UK could represent a true risk, although we suggest that it is more probable that respondents in the UK were more likely to complete the survey if their dog had experienced a GDV. The increased risk associated with being born in the 1990s may reflect the fact that younger dogs (those born in the 2000s) may go on to develop a GDV with age, or that a person completing the survey for a dog without a GDV was more likely to report on a currently owned dog, whereas the GDV dogs may have been previously owned dogs. Alternatively, this increased risk associated with being born in the 1990s could be a reflection of a real decrease in incidence of GDV because of improved management, breeding strategies, or formulations of dog food. Of the personality-associated factors that have previously been reported to influence the occurrence of GDV, positive behavioral traits (ie, happy and easygoing temperament) and submissive behaviors (ie, to other dogs or people) were associated with a decreased risk of GDV; negative behavioral traits (ie, fearfulness or agitation in response to strangers or environmental changes) and aggression to people were associated with an increased risk of GDV.

In the present study, there was a small but significant association between GDV and owner assessment of the dog's anxiety. The difference in anxiety scores between GDV cases and controls is unlikely to be able to be detected clinically because of the simplistic scoring system that we employed in the survey; however, given the large number of dogs included in the survey, this factor was determined to be significant. More detailed anxiety evaluation should be considered in future studies. Commercial dry dog food was also identified as a risk factor in our model. This finding is consistent with a study of acute gastric dilatation in young Irish Setters. It is unknown if this risk is associated with the tendency for the kibble to expand, added weight of a kibble meal, the influence on gastric emptying, or some other management feature of feeding kibble. In a study evaluating the influence of dietary composition on gastric emptying and motility in healthy large-breed dogs fed once daily, gastric postprandial motility and emptying were not affected by dietary composition (canned meat–based formula, dry cereal–based formula, dry cereal–based formula mixed with water). Unlike the study in Irish Setters, the frequency of feeding did not influence our model. Dogs that were predominantly pets (as opposed to performance or show dogs) and spent at least 5 hours a day with their owners were at higher risk for GDV requiring surgery. Our findings could be influenced by dog-specific factors such as fitness and activity levels and management factors associated with more extensive contact. In 1 study, large-breed dogs who attended dog shows had decreased risk of GDV in univariate analysis; however, this protective effect was not significant in the final proportional hazards risk model. There was no detectable influence of body condition score in the present study; however, owner assessment of body condition may not have been as objective as that of a trained professional. In addition, potentially stressful changes in environment that might influence the amount of time spent with the dog, such as a new person (eg, baby) or dog in the house could not be evaluated in this model.

The major categories of management that were associated with a decreased risk for GDV in the present study were dietary supplements and activity. The addition of eggs or fish to the food was associated with a decreased risk of GDV. The mechanism by which these, but not other supplements (eg, cod liver oil, vitamins, cooked or raw chicken, cheese, yogurt, or coat enhancers) were associated with a decreased risk of GDV is unknown. Supplemented dry dog food with table food was previously recommended to decrease the risk of GDV, but feeding table scraps had no significant effect in our study. Moderate physical activity can improve gastric emptying and accelerate intestinal transit of chyme and fecal residues and intraluminal gas in people; severe, exhaustive exercise, however, inhibits gastric emptying, interferes with gastrointestinal absorption, and causes many gastrointestinal symptoms, most notably gastrointestinal bleeding. This beneficial effect of moderate activity on gastrointestinal motility could potentially explain the observed protective effect in GDV dogs that spent equal time indoors and outdoors (versus primarily indoors or primarily outdoors) and likely had higher levels of physical activity. Postprandial exercise has been implicated in dogs as a risk factor for GDV, and recommendations have been made that intense physical activity should be restricted for 2 hours after meals. Contrary to expectations, in a prospective cohort study of 1,637 show dogs, restricting exercise before and after eating was found to increase the risk of GDV in large-breed dogs but not in giant-breed dogs (univariate analyses); those authors concluded that there was no advantage in restricting exercise before or after eating. In agreement with the latter study, dogs with GDV in the present study that were allowed to play with other dogs or run the fence after eating had a significantly decreased risk of GDV. Interestingly, the time of activity after eating had no impact on the GDV risk. On the basis of the results of our study and the study from Glickman et al., moderate physical activity after a meal may decrease the risk of GDV. It is also possible that owners of dogs that are perceived to be at higher risk because of familial tendencies or conformation toward GDV are hypervigilant and are more likely to restrict their dog's activity, thereby introducing a bias against restricting activity. Unfortunately, we were unable to evaluate fa-
milial tendencies toward GDV in this analysis because of the frequency of unanswereds questions regarding GDV in relatives of the dog of interest. Since this was an owner-based survey, we did not have a means to quantify chest depth or conformation. Consistent with Glickman et al.,7 females overall had a decreased risk of GDV, compared with males in our study. However, sexually intact female dogs were at increased risk of GDV. This dichotomy warrants investigation into factors that might be associated with sexually intact females, such as hormonal status and breeding history.

Many of our findings were consistent with other studies3,7,10 in that affected dogs were middle aged (median, 6 years), and the predominant breeds affected were German Shepherd Dog, Great Dane, Standard Poodle, and Doberman Pinscher. However, the present study differs from previous epidemiological studies evaluating risk factors for GDV in several ways. First, our study included > 2,500 dogs, of which > 1,000 had a GDV treated surgically, providing the power to detect relatively small differences. Second, in contrast to some of the previous studies that focused on unique populations of dogs (eg, show dogs and military working dogs) the majority of the dogs in our study were considered to be family pets. Third, we used a Web-based survey that enabled a fast worldwide distribution and entry of data.

The interpretation of our results needs to be considered within the limitations of our study. First, this was an owner-based survey. Survey responses about the dog could have been influenced by the owners’ own perceptions or memory of facts that were not necessarily true for the dog (eg, outside temperature), wrong assumptions (eg, of what a normal dog’s behavior or a normal body condition score is), sense of guilt, and recall bias. Another limitation is that the respondents were not required to answer all the questions, and therefore, not all of the data were collected and available for analysis. Additionally, people who owned dogs that were genetically or conformationally at risk for GDV may have been more likely to engage in practices that have been recommended to reduce the risk of GDV than owners of dogs that were not as predisposed to GDV. Therefore, the increased calculated risk of these practices may simply reflect the fact that these practices do not decrease the risk in dogs with other predisposing factors. Lastly, because of the nature of our study, we cannot guarantee that all patients reported as having GDV were true acute GDV cases.

The results of the present study have potential impact for general practitioners, emergency clinicians, and surgeons providing counseling for dog owners on the long-term management of dogs with a high risk for GDV. The most profound change in management would be relaxing the recommendations for activity restriction after meals. In addition, regular moderate outside activity should be encouraged because dogs that spent an equal amount of time indoors and outdoors had a decreased risk of GDV in this study. Dietary management appears to play an important role, and dry kibble may not be the best choice for dogs at risk for GDV; however, supplements with fish or eggs may reduce this risk. Our study was unable to show an association between GDV and feeding frequency, speed of eating, or eating from a height; therefore, no specific recommendations concerning these factors can be made at this time.

For owners and veterinarians, it is important to realize that despite multiple studies over the past 4 decades on the etiology of GDV, few consistent risk factors have been clearly identified; thereby making effective prevention very difficult. Owners of dogs at risk for GDV should be educated on the early recognition of the signs of GDV so that if their dog does develop GDV, prompt treatment can be pursued. Alternatively, until more definitive preventive strategies can be identified, prophylactic gastropexy in dogs at high risk for GDV can decrease morbidity and mortality.22,23

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**From this month’s *AJVR***

**Influence of P-glycoprotein modulation on plasma concentrations and pharmacokinetics of orally administered prednisolone in dogs**

Sara Van der Heyden et al

**Objective**—To evaluate the impact of modulation of the membrane-bound efflux pump P-glycoprotein (P-gp) on plasma concentrations of orally administered prednisolone in dogs.

**Animals**—7 healthy adult Beagles.

**Procedures**—Each dog received 3 treatments (control [no treatment], rifampicin [100 mg/d, PO, for 21 days, as an inducer of P-gp], and ketoconazole [100 mg/d, PO, for 21 days, as an inhibitor of P-gp]). A single dose of prednisolone (1 mg/kg, PO) was administered on day 8 of each treatment period. There was a 7-day washout period between subsequent treatments. Plasma concentrations of prednisolone were determined by use of a validated liquid chromatography–tandem mass spectrometry method. Duodenum and colon biopsy specimens were obtained endoscopically from anesthetized dogs and assessed for P-gp protein labeling via immunohistochemical analysis and mRNA quantification via real-time PCR assay. Total fecal collection was performed for evaluation of effects of P-gp modulation on digestion of nutrients.

**Results**—Rifampicin treatment upregulated duodenal P-gp in dogs and significantly reduced the area under the plasma concentration-time curve of prednisolone. Ketoconazole typically downregulated expression of duodenal P-gp, with a subsequent increase in the area under the plasma concentration-time curve of prednisolone. There was a noticeable interindividual difference in response. Digestion of nutrients was not affected.

**Conclusions and Clinical Relevance**—Modulation of P-gp expression influenced plasma concentrations of prednisolone after oral administration in dogs. Thus, treatment response to prednisolone may be influenced by coadministration of P-gp–modulating medications or feed ingredients. *(Am J Vet Res 2012;73:900–907)*