Serum alkaline phosphatase activity in Scottish Terriers versus dogs of other breeds

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Objective—To determine whether Scottish Terriers have higher serum alkaline phosphatase (ALP) activities and a higher prevalence of diseases commonly associated with high serum ALP activity than do dogs of other breeds.

Design—Retrospective case-control study.

Animals—85 Scottish Terriers and 340 age-matched control dogs that were not Scottish Terriers.

Procedure—Medical records were reviewed, and data for year of evaluation, age, sex, breed, serum ALP activity, and final diagnosis were recorded.

Results—Scottish Terriers had a significantly higher mean serum ALP activity than did control dogs (1,520 U/L vs 306 U/L). Regardless of breed, dogs that had a disease commonly associated with high serum ALP activity had a significantly higher mean serum ALP activity than did dogs without such diseases (1,304 U/L vs 427 U/L). Scottish Terriers were 2.4 times as likely to have a disease commonly associated with high serum ALP activity than were control dogs, but Scottish Terriers with diseases commonly associated with high serum ALP activity had a significantly higher mean ALP activity than did control dogs with such diseases (2,073 U/L vs 909 U/L), and Scottish Terriers without such diseases had a significantly higher mean serum ALP activity than did control dogs without such diseases (1,349 U/L vs 228 U/L).

Conclusions and Clinical Relevance—Results suggest that Scottish Terriers have higher serum ALP activities than do dogs of other breeds. Although Scottish Terriers also have a higher prevalence of diseases associated with high serum ALP activity, this alone did not explain the higher mean serum ALP activity in the breed. (J Am Vet Med Assoc 2006;228:222–224)

Alkaline phosphatase is an enzyme that is found in many tissues in the body. In dogs, bone, liver, and corticosteroid-induced isoenzymes of ALP all contribute to total serum ALP activity. Although the intestines are a source of ALP in many mammalian species, the intestinal ALP isoenzyme does not substantially contribute to serum ALP activity in dogs, most likely because of its short half-life. In young dogs, most serum ALP activity is a result of the bone isoenzyme. As dogs age, a greater portion of serum ALP activity is comprised of liver and corticosteroid-induced isoenzymes.

Many hepatic and nonhepatic disorders can cause high serum ALP activities in dogs, including hyperadrenocorticism, diabetes mellitus, primary hepatopathies, and pancreatitis. As a result, high serum ALP activity in an adult dog is usually considered indicative of an underlying pathologic process and will typically prompt a search for the underlying cause. It has been suggested that Scottish Terriers commonly have high serum ALP activities, often without appreciable clinical signs. To our knowledge, however, no data have been published to support this suggestion. This presents a dilemma as to how aggressively a finding of a high serum ALP activity should be pursued in a Scottish Terrier. The purpose of the study reported here, therefore, was to determine whether Scottish Terriers have higher serum ALP activities and a higher prevalence of diseases commonly associated with high serum ALP activity than do dogs of other breeds.

Materials and Methods

Study design—The study was designed as a retrospective, matched, case-control study. All dogs examined at the Michigan State University Veterinary Teaching Hospital between 1992 and 2002 in which a serum biochemical profile had been performed were considered for inclusion in the study. Dogs identified as Scottish Terriers were selected as cases. Four control dogs identified as any breed other than Scottish Terrier were matched to each case dog on the basis of age and year during which the serum biochemical profile was performed. Case and control dogs were matched on the basis of age because preliminary analyses revealed that serum ALP activity increased with age in Scottish Terriers and were matched on the basis of year during which the serum biochemical profile was performed because laboratory assay methods might have changed during the 10-year period of the study. Four control dogs were matched to each case dog to increase the power of the study.

Data collection—The following data were extracted from medical records for case and control dogs included in the study: year of evaluation, age, sex, breed, serum ALP activity, and final diagnosis as determined by the attending clinician. Serum ALP activity reflected total serum activity. Because of the retrospective nature of the study, individual isoenzyme activities were not available.

Statistical analysis—Descriptive statistics were generated for serum ALP activity and dog breed. For purposes of the present study, disorders commonly associated with high serum ALP activity were defined as hyperadrenocorticism, diabetes mellitus, pancreatitis, and hepatic disease of any kind. Analysis of variance and Wilcoxon rank sum tests were used to determine whether serum ALP activity was significantly associated with breed, age, or the presence of any disease commonly associated with high serum ALP activity. The Mantel-Haenszel χ²
test was used to determine whether Scottish Terriers were more likely to have any of the diseases associated with high serum ALP activity than were dogs of other breeds. Multivariable ANOVA was used to test whether serum ALP activity was associated with breed, the presence of any disease commonly associated with high serum ALP activity, and the interaction between breed and the presence of any such disease. All statistical analyses were performed with standard software. Values of P < 0.05 were considered significant. The reference range for serum ALP activity in adult dogs reported by the Michigan State University clinical pathology laboratory during the time of the study was 14 to 104 U/L.

Results
Data were collected for 85 Scottish Terriers and 340 control dogs that were not Scottish Terriers. Dogs ranged from 1 to > 11 years old. Of the 340 control dogs, 103 were of mixed breeding, with the remainder representing 64 breeds. The 5 most common breeds among control dogs were Labrador Retriever (n = 25), Cocker Spaniel (22), Golden Retriever (16), German Shepherd Dog (13), and Miniature Schnauzer (10).

Scottish Terriers had a significantly (P < 0.001) higher mean serum ALP activity (mean ± SD, 1,520 ± 2,010 U/L) than did control dogs (306 ± 697 U/L). Regardless of breed, dogs that had a disease commonly associated with high serum ALP activity (ie, hyperadrenocorticism, diabetes mellitus, pancreatitis, or hepatic disease of any kind) had a significantly (P < 0.001) higher mean serum ALP activity (1,304 ± 1,951 U/L) than did dogs without such diseases (427 ± 972 U/L). Serum ALP activity significantly increased with age in Scottish Terriers but not in control dogs (Table 1).

Twenty of the 85 (23.5%) Scottish Terriers had a disease associated with high serum ALP activity, whereas only 39 of the 340 (11.5%) control dogs did, and Scottish Terriers were 2.4 times as likely (95% confidence interval, 1.3 to 4.3) to have a disease associated with high serum ALP activity as were the control dogs. For both Scottish Terriers and the control dogs, age was not significantly (P = 0.176 and P = 0.930, respectively) associated with whether dogs had a disease associated with high serum ALP activity.

When controlling for age of the dog and year during which serum ALP activity was measured, breed (Scottish Terrier vs any other breed) and presence of a disease associated with high serum ALP activity (yes vs no) were both significantly (P < 0.001) associated with serum ALP activity. Scottish Terriers with diseases commonly associated with high serum ALP activity had a significantly (P = 0.029) higher mean serum ALP activity (mean ± SD, 2,073 ± 2,567 U/L) than did control dogs with such diseases (900 ± 1,795 U/L). Similarly, Scottish Terriers without such diseases had a significantly (P < 0.001) higher mean serum ALP activity (1,349 ± 1,430 U/L) than did control dogs without such diseases (228 ± 487 U/L).

Discussion
Results of the present study suggest that Scottish Terriers have higher serum ALP activities than do dogs of other breeds, regardless of age or the presence of certain disorders commonly associated with high serum ALP activity (ie, hyperadrenocorticism, diabetes mellitus, pancreatitis, and hepatic disease of any kind). In addition, although Scottish Terriers also had a higher prevalence of diseases associated with high serum ALP activity, this alone did not explain the higher mean serum ALP activity in the breed.

Potential underlying mechanisms for high serum ALP activity in a dog include increased synthesis, increased release from tissue into serum, reduced clearance, or some combination of these factors. Several possibilities exist for the higher serum ALP activity in Scottish Terriers. One is simply that this is a normal situation for Scottish Terriers and may represent greater expression by unidentified tissues, either physiologically or pathologically. Another possibility is that Scottish Terriers have a higher prevalence of certain hepatopathies that result in cholestatic damage. These may include infectious, neoplastic, or immune-mediated processes that are not well understood.

It is unclear why there was an age-related increase in serum ALP activity in Scottish Terriers in the present study, but a similar age-related increase has been documented in people and is also not completely understood. Whether the observed increase in serum ALP activity in Scottish Terriers, compared with dogs of other breeds, is similar to the reported benign familial hyperphosphatemia of Siberian Huskies is unclear, but the hyperphosphatemia of Siberian Husky puppies has not been reported to be progressive with age. It has been proposed by others that Scottish Terriers might have a higher prevalence of adrenal hyperplasia that results in production of aberrant adrenal steroids, such as progesterone or 17-hydroxyprogesterone, that are not routinely identified in the workup of patients suspected to have hyperadrenocorticism.

The present study was limited by the fact that analyses were performed retrospectively on dogs exam-

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Table 1—Serum ALP activity as a function of age in Scottish Terriers and dogs of other breeds.

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (y)</th>
<th>No. of dogs</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scottish Terriers*</td>
<td>1–6</td>
<td>15</td>
<td>465</td>
<td>432</td>
</tr>
<tr>
<td></td>
<td>7–8</td>
<td>25</td>
<td>1,156</td>
<td>1,363</td>
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<td></td>
<td>9–10</td>
<td>21</td>
<td>1,873</td>
<td>2,024</td>
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<tr>
<td></td>
<td>&gt; 11</td>
<td>24</td>
<td>2,249</td>
<td>2,756</td>
</tr>
<tr>
<td>Dogs of other breeds</td>
<td>1–6</td>
<td>60</td>
<td>312</td>
<td>883</td>
</tr>
<tr>
<td></td>
<td>7–8</td>
<td>96</td>
<td>264</td>
<td>732</td>
</tr>
<tr>
<td></td>
<td>9–10</td>
<td>94</td>
<td>296</td>
<td>419</td>
</tr>
<tr>
<td></td>
<td>&gt; 11</td>
<td>90</td>
<td>356</td>
<td>757</td>
</tr>
</tbody>
</table>

*Serum ALP activity increased significantly (P = 0.030) with age.
indeed at a veterinary teaching hospital. Because the teaching hospital was predominantly a referral practice, it can be assumed that most patients had some underlying illness. Although certain diseases have a direct effect on serum ALP activity, any underlying disorder could have resulted in a stress response, which in turn could potentially have increased serum ALP activity. To the extent possible, this limitation was addressed by comparing Scottish Terriers with a control population of dogs other than Scottish Terriers that were examined at the same veterinary teaching hospital and therefore would be expected to have the same underlying illnesses and attendant stresses. Whether clinically normal Scottish Terriers that are not examined at a veterinary teaching hospital also have high serum ALP activity is unknown. A population-based, prospective study evaluating clinically normal Scottish Terriers would increase the external validity of our findings.

Despite its limitations, there are also several strengths to the present study. First, matching 4 controls to each case increased the power of the study. Second, controlling for age, year during which serum biochemical testing was performed, and the presence of diseases associated with high serum ALP activity increased the likelihood that a real difference in serum ALP activity between Scottish Terriers and dogs of other breeds would be detected. Third, the sample size was large, increasing the internal validity of the study.

In the present study, we found that serum ALP activity increases with age in Scottish Terriers and that Scottish Terriers, irrespective of age, have higher serum ALP activity than do dogs of other breeds. Additional studies are required to determine the cause of high serum ALP activity in Scottish Terriers, such as histologic evaluation of liver biopsy samples, measurement of ALP isoenzyme activities, and evaluation of adrenal gland function.

References