Breed Associations for Canine Exocrine Pancreatic Insufficiency

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Background: Knowledge of breed associations is valuable to clinicians and researchers investigating diseases with a genetic basis.

Hypothesis: Among symptomatic dogs tested for exocrine pancreatic insufficiency (EPI) by canine trypsin-like immunoreactivity (cTLI) assay, EPI is common in certain breeds and rare in others. Some breeds may be overrepresented or underrepresented in the population of dogs with EPI. Pathogenesis of EPI may be different among breeds.

Animals: Client-owned dogs with clinical signs, tested for EPI by radioimmunoassay of serum cTLI, were used.

Methods: In this retrospective study, results of 13,069 cTLI assays were reviewed.

Results: An association with EPI was found in Chows, Cavalier King Charles Spaniels (CKCS), Rough-Coated Collies (RCC), and German Shepherd Dogs (GSD) (all P < .001). Chows (median, 16 months) were younger at diagnosis than CKCS (median, 72 months, P < .001), but not significantly different from GSD (median, 36 months, P = .10) or RCC (median, 36 months, P = .16). GSD (P < .001) and RCC (P = .015) were younger at diagnosis than CKCS. Boxers (P < .001), Golden Retrievers (P < .001), Labrador Retrievers (P < .001), Rottweilers (P = .002), and Weimaraners (P = .002) were underrepresented in the population with EPI.

Conclusions and Clinical Implications: An association with EPI in Chows has not previously been reported. In breeds with early-onset EPI, immune-mediated mechanisms are possible or the disease may be congenital. When EPI manifests later, as in CKCS, pathogenesis is likely different (eg, secondary to chronic pancreatitis). Underrepresentation of certain breeds among dogs with EPI has not previously been recognized and may imply the existence of breed-specific mechanisms that protect pancreatic tissue from injury.

Key words: Dog; Pancreas; Malabsorption; Trypsin-like immunoreactivity.

B reed associations are well established for many canine diseases, and this knowledge is useful for clinicians. If a particular breed has a known association with a disorder, tests can be prioritized to confirm or eliminate that possibility at the earliest opportunity. Similarly, when a disease is rare in a particular breed, unnecessary investigations can be avoided, saving time and expense. Identifying breed associations is also an important first step when studying the etiopathogenesis of disorders with a known or suspected genetic basis, and, in conjunction with data from the canine genome project, candidate genes of interest can be identified. Therefore, insights into breed associations may be gathered by large-scale epidemiologic surveys.

Canine exocrine pancreatic insufficiency (EPI) is a disease characterized by inadequate production of digestive enzymes from pancreatic acinar cells, which causes characteristic clinical signs including polyphagia, weight loss, and increased fecal volume with poorly digested, loose feces. Pathologic processes that may lead

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Submitted April 28, 2006; Revised August 15, 2006, October 3, 2006, October 9, 2006; Accepted November 7, 2006.

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0891-6640/07/2102-0001/\$3.00/0

to EPI in dogs include pancreatic acinar atrophy (PAA), chronic pancreatitis, pancreatic hypoplasia, and pancreatic neoplasia. PAA is reported to be the most common cause of EPI in dogs, and German Shepherd Dogs (GSD) are known to be predisposed. In this breed, PAA is inherited in an autosomal recessive manner and may be autoimmune in origin.1-7 PAA is also inherited in Rough-Coated Collies (RCC), and is again presumed to be autoimmune.⁵⁻⁸ EPI has been reported in other breeds. and EPI in related English Setters in Italy has been described.9 Cases of EPI caused by chronic pancreatitis (CP) have been reported, but given the difficulties with diagnosis, CP may be a more common cause of EPI in dogs than is currently recognized. 10,11 There are strong breed associations with CP in the Cavalier King Charles Spaniel (CKCS) and Jack Russell Terrier.^a

Diagnosis of EPI is based on typical history and clinical signs and is confirmed by pancreatic function testing. ¹² Measurement of canine serum trypsin-like immunoreactivity (cTLI) by radioimmunoassay (RIA) is both highly sensitive and highly specific for EPI. ¹³ The Comparative Gastroenterology Laboratory, Department of Veterinary Pathology, University of Liverpool was one of the first laboratories to develop a RIA for cTLI, and this assay was offered commercially between the years of 1983 and 2005. This has generated a database of more than 13,000 cTLI assay results.

The authors hypothesized that important breed associations exist for canine EPI, and that among dogs with clinical signs of gastrointestinal disease undergoing cTLI assay, EPI is common in certain breeds and rare in others. Furthermore, certain breeds may be overrepresented or underrepresented within the population affected by EPI. The main objectives of this retrospective study were to compare the proportion of tests positive for EPI among breeds in a large population of clinically affected dogs undergoing cTLI assay and to

208 Batchelor et al

compare the relative proportion of each breed in this affected population with that in a large control population.

Materials and Methods

Study Population

Results of all cTLI assays submitted to the Comparative Gastroenterology Laboratory, University of Liverpool between January 1990 and September 2002 were reviewed. Dogs with a serum cTLI concentration of <2.5 µg/L were considered to be affected by EPI. In total, records for 13,069 dogs were included.

Detection of Candidate Overrepresented and Underrepresented Breeds

Two methods were employed to identify individual breeds overrepresented or underrepresented in the population of dogs with EPI:

Analysis within the Sampled Population. To avoid spurious results from breeds in which few individuals were sampled, only breeds for which at least 30 individuals were tested were assessed. This cut-off was chosen because it represented approximately 1/500th (0.2%) of the database. For each breed, observed prevalence of EPI (proportion of dogs with EPI in the population sampled) with 95% confidence interval (CI) was calculated and compared to the proportion of dogs with EPI in the whole sampled population. GSD were excluded from this calculation because of the large number sampled and the high observed breed prevalence. Thus, observed prevalence of EPI was calculated for the whole population minus GSD (within-data control population). Breeds for which the 95% CI did not overlap with the 95% CI for the within-data control population were considered potentially overrepresented or underrepresented in the population of dogs with EPI.

Comparison with the Pet Dog Population as a Whole. A database of 47,957 insured dogs (representing animals insured in 2003) was chosen as a control population, to provide an approximation of the United Kingdom pet dog population. The commercial company that provided the records offers health insurance for companion animals; the service is voluntary, and most animals are insured throughout their life. For each breed, the proportion of the affected population (all dogs with EPI in the TLI database) was calculated and compared with the proportion of the same breed within the insured dog population (control population). Breeds were considered potentially overrepresented or underrepresented when the proportion within the population of dogs with confirmed EPI was significantly different from the corresponding proportion in the insurance database.

Where a breed was identified as overrepresented by both methods, evidence was considered to exist for a genuine association with EPI. Where a breed was identified as underrepresented by both methods, evidence was considered to exist that EPI may occur less frequently in that breed.

Data Handling and Statistical Analysis

Data were entered into a statistical software program. Categorical variables, such as breed proportions in affected and control populations, were compared by χ^2 analysis. Sex was known for most dogs, and χ^2 analysis was used to examine possible differences. Because neuter status was not recorded, the effect of neutering was not examined. Requirements for using parametric tests for age comparisons were not met, so initial comparison of age at diagnosis among breeds was by the Kruskal-Wallis method.

Ages at diagnosis among individual breeds were further explored with post-hoc testing using the Mann-Whitney U test. Significance was set at P < .05.

Results

Study Population

Records for 13,069 cTLI assays were reviewed. Dogs of 132 breeds were tested; 52 breeds were represented by >30 individuals. There were 3,537 GSD sampled (28.8% of the sampled population). In total, 1,127/13,069 dogs (8.6%; 95% CI: 8.1% to 9.1%) were diagnosed with EPI (TLI < 2.5 µg/L). EPI was detected in 59 different breeds.

Analysis by Breed within the Sampled Population

Breed was known for 12,259 dogs, of which 1,064 had EPI. The proportion of dogs with EPI in the whole population sampled, where breed was known, was 8.7% (95% CI: 8.2% to 9.2%), although this value was skewed by the large number of GSD sampled. The proportion of dogs with EPI in the within-data control population (whole population excluding GSD) was 4.9% (95% CI: 4.4% to 5.4%).

Observed prevalence of EPI in Chows, CKCS, GSD, West Highland White terriers (WHWT), Cocker Spaniels, RCC, and mixed breed dogs in the sampled population was significantly higher than in the withindata control population (Table 1, Fig 1). The Corgi and Cairn Terrier breeds also were identified as overrepresented, although there were few affected individuals of these breeds. Observed prevalence in the Jack Russell Terrier was not significantly different from control (Table 2).

Observed prevalence in Boxers, Great Danes, Golden Retrievers, Labrador Retrievers, Rottweilers, and Weimaraners was significantly lower in the sampled population than in the within-data control population (Table 1, Fig 1), most notably in Boxers where, of 524 individuals tested, none had EPI.

Comparison with a Database of Insured Dogs

Data are summarized in Table 3. When compared with the pet insurance database, GSD, CKCS, Chows, and RCC were overrepresented in the affected population (all P < .001). Corgis also were overrepresented, although there were few affected dogs. Boxers (P < .001), Golden Retrievers (P < .001), Labrador Retrievers (P < .001), Rottweilers (P = .022), and Weimaraners (P = .002) were underrepresented in the affected population. Mixed breed dogs also were underrepresented (P < .001). The proportions of WHWT (P = .47), Cocker Spaniels (P = .10), Cairn Terriers (P = .22), and Great Danes (P = .23) were not significantly different among populations.

Summary of Breed Trends Identified

By both methods of comparison, Chows, CKCS, GSD, and RCC were overrepresented, and Boxers, Golden

Table 1. Observed prevalence (and 95% confidence interval) of exocrine pancreatic insufficiency in breeds where increased or decreased prevalence was observed.

				95% Confidence Interval	
Breed	Number Affected	Number Tested	Observed Prevalence ^a	Lowera	Upper ^a
Whole population					
All	1,064	12,259	8.7	8.2	9.2
All breeds excluding German Shepherd Dogs	427	8,722	4.9	4.4	5.4
Breeds with increased prevalence					
Chow	24	38	63.2	46.0	78.2
Cavalier King Charles Spaniel	64	243	26.3	20.9	32.3
German Shepherd Dog	637	3,537	18.0	16.8	19.3
Corgi	6	36	16.7	6.4	32.8
Cairn Terrier	8	49	16.3	7.3	29.7
West Highland White Terrier	43	273	15.8	11.6	20.6
Cocker Spaniel	23	181	12.7	8.2	18.5
Rough-Coated Collie	15	144	10.4	5.9	16.6
Mixed breed	93	1093	8.5	6.9	10.3
Breeds with decreased prevalence					
Boxer	0	524	0.0	0.0	0.6
Golden Retriever	1	763	0.1	0.0	0.7
Great Dane	1	192	0.5	0.0	2.9
Rottweiler	1	220	0.5	0.0	2.5
Labrador Retriever	9	889	1.0	0.5	1.9
Weimaraner	2	181	1.1	0.1	3.9

^a Prevalence data are expressed as percentages.

Retrievers, Labrador Retrievers, Rottweilers, and Weimaraners were underrepresented in the affected population.

Age

Age was known for 1,023 affected dogs. Overall median age at diagnosis was 42 months (range, 3–204); the ages of dogs with EPI in each predisposed breed are illustrated in Figure 2. The Kruskal-Wallis test demonstrated significant differences in age at diagnosis among breeds (P < .001). Posthoc analysis with the Mann-Whitney test demonstrated that CKCS were older at the time of diagnosis (median, 72 months; range, 24–156) than GSD (median, 36 months; range, 6–204, P < .001), Chows (median, 16 months; range, 7–108, P < .001), and RCC (median, 36 months; range, 12–132, P = .015). Age at diagnosis was not significantly different between Chows and GSD (P = .10) or RCC (P = .16).

Sex Trends

Male dogs were overrepresented in the sampled population (58.8%). However, females were overrepresented among the affected dogs (602/1,063 female, 56.6%; P < .001). Overrepresentation of females was seen in Chows (19/24 female, 79%; P = .007), CKCS (39/64 female, 61%; P = .005), and GSD (312/614 female, 50.8%; P < .001). In the RCC, no sex association was observed (7/15 female; P = .80).

Discussion

In this study, breed associations were investigated for canine EPI. Evidence was found for novel breed associations in EPI, and it was also found that EPI is uncommon in certain other breeds. Such information may be valuable to clinicians: for example, the cTLI test could be prioritized in breeds known to be predisposed to EPI. This is already likely to occur for some breeds (eg, GSD), and may in part explain why so many of this breed were included in the sample population. However, this work should enable a similar strategy to be employed for the other breeds identified as overrepresented. These data also suggest differences in the pathogenesis of EPI among different breeds and therefore may inform future research projects into etiopathogenesis, treatment, and prevention. For example, where EPI is known or suspected to be caused by chronic pancreatitis, risk factors such as obesity and feeding a high-fat diet can be minimized. In contrast, where there is a known or suspected genetic association (eg, in GSD and RCC), breeding programs could ultimately be devised to eliminate the problem from the breed. It is not yet known whether the associations in this study are representative of other parts of the world and, until more work is available, veterinarians should be cautious in extrapolating the information to other countries.

The main strengths of this retrospective study are the robust nature of the cTLI test and the number of results (13,069) available for analysis. cTLI measurement is unaffected by intestinal disease, and a serum cTLI concentration <2.5 μ g/L is consistent with EPI, with sensitivity and specificity approaching 100%.¹³ The number of dogs tested meant that, for many breeds, sufficient dogs had been tested to provide useful data on the signalment of dogs affected by EPI.

210 Batchelor et al

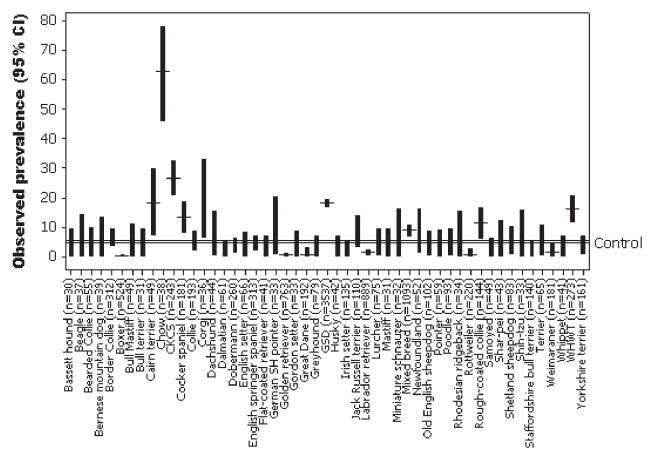


Fig 1. Observed prevalence (vertical bars) and 95% confidence interval (extremities of boxes) of exocrine pancreatic insufficiency in the sampled dogs of each breed, compared to the within-data control population. CKCS, Cavalier King Charles Spaniel; GSD, German Shepherd Dog; German SH Pointer, German Short-haired Pointer; WHWT, West Highland White Terrier.

However, this approach also has limitations. First, we were reliant on information provided by the veterinarians submitting the samples. Patient data were sometimes incomplete; specifically, some breed names were abridged (eg, collie, retriever, spaniel, and setter) and could not be included in the analysis of breed associations. This may have contributed to the limited number of results available for the RCC and might explain why only a weak association was found in this breed.

Second, obtaining an ideal control population of dogs for comparison is difficult, and the observed frequency of each breed in the affected population is affected by its relative popularity. This study aimed to overcome these problems by comparing breeds in 2 ways. First, we performed a within-database comparison, comparing the observed prevalence (proportion of tested dogs positive for EPI) in each breed with that in all dogs sampled. For these calculations, GSD were excluded from the control population because the large number of GSD sampled and their high observed prevalence of EPI would have had a considerable skewing effect on the data. This within-database comparison is not perfect because an apparent increase in observed prevalence can either be because the breed is genuinely predisposed to EPI or because other diseases that cause the same constellation of signs are less common. Similarly, an apparent decrease in observed prevalence actually may be because other diseases causing similar signs are more common. This first comparison still is useful because it provides information on the population the veterinarian is testing (ie, dogs with alimentary tract disease). At the very least, it may give an index of suspicion as to the likelihood of EPI in an individual dog with suspicious clinical signs.

Because the within-database comparison alone was insufficient to prove genuine breed associations, a second comparison was performed, this time by relating the cases diagnosed with EPI with a database of insured dogs in the UK. This database, although not perfect, provided an approximation of breed trends within the UK dog population. This database may not be fully representative, because not all dogs in the UK are insured and a number of companies offer pet insurance. Furthermore, there may be differences in the tendency for owners of different types of dog (ie, pedigree versus mixed breed) to take out insurance. However, studies from Sweden have already validated the use of pet insurance records in prevalence studies, and this population was demonstrated to be representative of the dog population in Sweden. 14,15 Furthermore, the database used in this study previously has been used in a study on the prevalence of canine diabetes mellitus.¹⁶

Table 2. The observed prevalence (and 95% confidence interval) of exocrine pancreatic insufficiency in all remaining breeds where ≥30 individuals had been tested.

Breed			Observed Prevalence ^a	95% Confidence Interval	
	Number Affected	Number Tested		Lowera	Uppera
Basset Hound	0	30	0.0	0.0	9.5
Bearded Collie	1	55	1.8	0.0	9.7
Beagle	1	37	2.7	0.1	14.2
Bernese Mountain Dog	1	39	2.6	0.1	13.5
Border Collie	19	312	6.1	3.7	9.3
Bull Mastiff	1	49	2.0	0.1	10.9
Bull Terrier	0	31	0.0	0.0	9.2
Collie (unspecified)	9	193	4.7	2.2	8.7
Dachshund	2	44	4.5	0.6	15.5
Dalmatian	0	61	0.0	0.0	4.8
Dobermann Pinscher	8	260	3.1	1.3	6.0
English Setter	1	66	1.5	0.0	8.2
English Springer Spaniel	13	313	4.2	2.2	7.0
Flat-coated Retriever	0	41	0.0	0.0	7.0
German Short-haired Pointer	2	33	6.1	0.7	20.2
Gordon Setter	0	33	0.0	0.0	8.7
Greyhound	1	79	1.3	0.0	6.9
Husky	0	42	0.0	0.0	6.9
Irish Setter	2	135	1.5	0.2	5.2
Jack Russell Terrier	8	110	7.3	3.2	13.8
Lurcher	2	75	2.7	0.3	9.3
Other breed ^b	21	663	3.2	2.0	4.8
Mastiff	0	31	0.0	0.0	9.2
Miniature Schnauzer	1	32	3.1	0.1	16.2
Newfoundland	3	52	5.8	1.2	15.9
Old English Sheepdog	3	102	2.9	0.6	8.4
Pointer	1	59	1.7	0.0	9.1
Poodle	3	93	3.2	0.7	9.1
Rhodesian Ridgeback	1	34	2.9	0.1	15.3
Samoyed	0	49	0.0	0.0	5.9
Shar-pei	1	43	2.3	0.1	12.3
Shetland Sheepdog	3	83	3.6	0.8	10.2
Shih-tzu	1	33	3.0	0.1	15.8
Staffordshire Bull Terrier	2	140	1.4	0.2	5.1
Terrier (unspecified)	2	65	3.1	0.4	10.7
Whippet	0	41	0.0	0.0	7.0
Yorkshire Terrier	5	161	3.1	1.0	7.1

^a Prevalence data are expressed as percentages.

However, given that less information exists about the national pet population in the UK, it is unclear how representative this database actually is, and conclusions must be drawn cautiously. An alternative would have been to compare results with UK Kennel Club records but, because only pedigree dogs are included, this population also is biased. Thus, although this control population was not perfect, it did represent a large control group, and the fact that, for most pedigree dog

breeds, there was close agreement between the 2 methods, suggests that this population was acceptable.

Mixed breed dogs were shown to be overrepresented when comparing with the within-database control (ie, dogs with alimentary tract signs), but underrepresented when comparing with the insurance database (ie, this estimate of the UK pet dog population). This implies that EPI is uncommon in the mixed breed population as a whole, but common in mixed breed dogs with

bOther breeds tested included Afghan Hound, Airedale Terrier, Japanese Akita, Alaskan Malamute, American Cocker Spaniel, Australian Terrier, Basenji, Bedlington Terrier, Belgian Shepherd Dog, Bernese Mountain Dog, Bichon Frise, Border Terrier, Borzoi, Boston Terrier, Bouvier des Flandres, Briard, Bulldog, Chesapeake Bay Retriever, Chihuahua, Curly-Coated Retriever, Miniature Dachshund, Wire-Haired Dachshund, Dandie Dinmont Terrier, Dogue de Bordeaux, English Pointer, Fox Terrier, Foxhound, French Bulldog, German Wirehaired Pointer, Hungarian Sheepdog, Irish Terrier, Irish Water Spaniel, Irish Wolfhound, Italian Spinone, Keeshond, Kerry Blue Terrier, Lakeland Terrier, Lancashire Heeler, Leonberger, Lhasa Apso, Maltese Terrier, Manchester Terrier, Miniature Pinscher, Neopolitan Mastiff, Norwegian Elkhound, Norwich Terrier, Otterhound, Papillon, Patterdale Terrier, Pekingese, Petit Basset Griffon Vendeen, Pharaoh Hound, Pit Bull Terrier, Pomeranian, Miniature Poodle, Toy Poodle, Pug, Puli, Pyrenean Mountain Dog, Saint Bernard, Saluki, Giant Schnauzer, Standard Schnauzer, Scottish Deerhound, Scottish Terrier, Sealyham Terrier, Skye Terrier, Smooth Collie, Soft-Coated Wheaten Terrier, Spitz, Tibetan Mastiff, Tibetan Spaniel, Tibetan Terrier, Vizsla, Welsh Springer Spaniel, and Welsh Terrier.

212 Batchelor et al

Table 3. Comparison of breed proportions among the population of dogs with exocrine pancreatic insufficiency and the control population.

	Population with EPI		Control Population ^a		
Breed	Number	0/0p	Number	0/0	P Value
Breeds where observed prevalence was	greater than control				
German Shepherd Dog	637	59.9	2,889	6.03	<.001
Cavalier King Charles Spaniel	64	6.0	1,390	2.90	<.001
West Highland White Terrier	43	4.0	2,160	4.51	.469
Chow	24	2.3	88	0.18	<.001
Cocker Spaniel	23	2.2	1,727	3.60	.10
Rough-Coated Collie	15	1.4	236	0.49	<.001
Cairn Terrier	8	0.8	232	0.48	.22
Corgi	6	0.6	77	0.16	.002
Breeds where observed prevalence was I	ess than control				
Boxer	0	0	1,933	4.03	<.001
Golden Retriever	1	0.1	2,990	6.24	<.001
Rottweiler	1	0.1	318	0.66	.022
Great Dane	1	0.1	141	0.29	.23
Weimaraner	2	0.2	598	1.25	.002
Labrador Retriever	9	0.8	6,780	14.1	<.001
Mixed breed	93	8.7	8,208	17.1	<.001

EPI, exocrine pancreatic insufficiency.

alimentary tract signs. The reason for this discrepancy is not clear; one possible explanation is that other causes of chronic alimentary tract disease (such as inflammatory bowel disease [IBD]) may be less common in mixed breed dogs. This is supported by the fact that genetic factors are involved in the pathogenesis of IBD, and

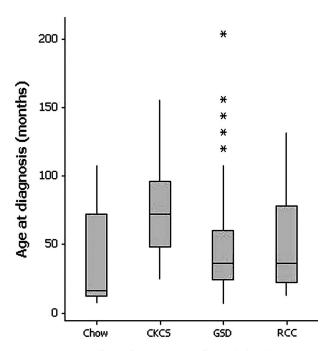


Fig 2. Age at diagnosis among predisposed breeds. CKCS, Cavalier King Charles Spaniel; GSD, German Shepherd Dog; Rough-Coated Collies (RCC). Shaded boxes show median (horizontal line) and interquartile range (top and bottom of box). Vertical lines show range (* = outliers).

numerous pedigree dog breeds are predisposed.¹⁷ Therefore, mixed breed dogs may be less likely to develop such chronic enteropathies. Further work would be required to determine the true prevalence of EPI and chronic enteropathies in mixed breed dogs.

Associations with EPI were found in Chows, CKCS, GSD, and RCC. For GSD and RCC, an association with EPI is already known. 1-8,18-21 CKCS were reported to be predisposed in a study from North America.d However, a breed association has not previously been recognized in Chows. Although not a commonly tested breed, of the Chows in this study undergoing serum cTLI assay, 63% were positive for EPI. The Chows were tested during a 13-year period, and samples were received from a wide geographical area, making it unlikely that a single predisposed family was tested, producing an anomalous result. Given the small number of dogs of this breed tested, it cannot necessarily be suggested that almost two thirds of Chows with compatible clinical signs are likely to have EPI; the true prevalence may not be that high. Other explanations would include the possibility that clinicians fail to consider this differential diagnosis for dogs of this breed. Whatever the true prevalence and the reasons behind it, this finding suggests that clinicians should prioritize testing for EPI when gastrointestinal signs are present in Chows. The high observed prevalence in CKCS could be interpreted in a similar manner, with similar caveats.

Chows were diagnosed with EPI at a relatively young age in comparison with most other breeds. Two of the main exceptions were GSD and RCC, breeds in which EPI is hereditary and autoimmune in nature.^{1–8} The age distribution of the Chow EPI cases argues for a similar

^a Control population for this comparison is a database of 47,957 insured dogs (data courtesy of Pet Protect Limited).

^b Number affected as % of the 1064 dogs tested where breed was known.

mechanism in this breed. Alternative mechanisms could include congenital disorders such as pancreatic hypoplasia.²² Further work to confirm the underlying mechanism would involve histopathologic assessment of pancreas specimens from affected (ideally subclinical) dogs and pedigree analysis.

In contrast, the median age at diagnosis in the CKCS was significantly older than in the GSD. This implies that a different pathogenesis is involved in this breed. CKCS are reportedly predisposed to CP,^a suggesting that ongoing uncontrolled pancreatic inflammation is the reason that they develop EPI. CP is also a common cause of EPI in cats and human beings and most frequently arises in middle age onward.^{23–25} As neither pancreatic biopsy nor postmortem examination was performed in this study, firm conclusions on causality in CKCS cannot be made and further work is required.

There was an overall female association with EPI, and a female association was seen in GSD, CKCS, and Chows, but not RCC. A female association with EPI exists in Finnish RCC. The fairly small number of RCC tested here means that an existing female association may have been missed. The association with females in GSD is interesting as the pattern of inheritance of PAA is suspected to be autosomal recessive. Other factors may be involved, with PAA more likely to progress to clinical EPI in females. Association with females also was seen in CKCS, in which a different pathogenesis is suspected. The reason for the female association in EPI is not known, and it may be that other factors are required for pancreatic injury to progress to EPI.

Underrepresentation of certain breeds in a population of dogs affected by EPI has not been reported previously. Most notable were the findings in Boxers where, despite their popularity in the UK (1,933/47,957 [4.0%] in the insurance database) and the large number of submissions for cTLI assay, no cases of EPI were found. EPI has been documented in Boxers in North America,^d and populations of Boxers in other countries will need to be assessed to verify this finding. Nevertheless, the findings are noteworthy because a decreased prevalence for diabetes mellitus also has been reported in Boxer dogs.16 A number of other breeds, including Golden Retrievers, Labrador Retrievers, Rottweilers, and Weimaraners were also underrepresented in the affected population. It is not known whether the mechanisms involved in protecting such breeds are similar or whether unique mechanisms are involved in each case. Studying the mechanisms behind this phenomenon may uncover novel therapeutic targets and new treatment modalities.

In conclusion, this study provides supportive evidence that GSD, RCC, and CKCS are predisposed and new evidence that Chows may also be predisposed to EPI. These breeds can be separated into 2 distinct groups depending upon age of onset. Age of onset may provide clues to the likely pathologic mechanisms. In breeds with early-onset disease an immune-mediated mechanism is possible or the disease may be congenital; where EPI manifests later, an alternative mechanism is likely (eg, secondary to CP). Finally, Boxers, Golden and Labra-

dor Retrievers, Rottweilers, and Weimaraners are less likely to develop clinical EPI than other breeds, although the reasons for this are not clear. Further studies will be required to investigate the genetic basis for the breed associations documented in this study.

Footnotes

- ^a Watson PJ, Roulois A, Johnston P et al. Prevalence of chronic pancreatitis in an unselected population of first opinion dogs. J Vet Intern Med 2005;19:948 (abstract)
- ^b Data courtesy of Pet Protect Limited, Furness House, 53 Brighton Road, Redhill, Surrey, RH1 6RD UK
- ^c Minitab v14.0; Minitab Inc, State College, PA
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Acknowledgments

DJB is funded by Hill's Pet Nutrition Ltd. AJG is funded by Royal Canin. The authors are grateful to the veterinarians who submitted samples for TLI assay, to Mr L.B. German for his help in data processing, and to Ruth Cottam and the staff at Pet Protect.

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214 Batchelor et al

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