

Prediction of future development of canine atopic dermatitis based on examination of clinical history

OBJECTIVES: The aim of this study was to identify clinical features that could be used to identify individual dogs within the Guide Dogs for the Blind Association canine population at risk of being diagnosed as atopic in the future before they had fully developed the condition.

METHODS: Clinical histories of atopic and non-atopic dogs from the Guide Dogs for the Blind Association population were analysed and statistically significant differences identified between the two groups.

RESULTS: Atopic dogs were consistently affected by skin disease at a younger age than non-atopic dogs and that there was a significant difference in event curves between atopic and non-atopic dogs at 10 months of age. From a predictive point of view, dogs that suffered from four or more episodes of atopic-type skin disease by the age of 15 months were at an increased risk of developing atopic dermatitis.

CLINICAL SIGNIFICANCE: It is suggested that the clinical history of all dogs from the Guide Dogs for the Blind Association about to undergo training should be examined for these factors to assess whether or not they should undergo training.

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INTRODUCTION

Atopic dermatitis is a common skin condition affecting dogs (among other species). The prevalence of this condition is much debated. Different surveys have shown that atopic dermatitis is either the most common (Scott and Paradis 1990) or the second most common cause of canine pruritus (Scott and others 2001, reviewed in Hillier and Griffin 2001).

Particular breeds are known to be more likely to develop atopic dermatitis, including the Labrador/golden retriever, English setter, West Highland white terrier and English/Staffordshire bull terrier.

As mentioned above, the main clinical feature of atopic dermatitis is pruritus. This is mainly concentrated on the ears,

eyes and feet with the resultant development of otitis externa, conjunctivitis and pedal dermatitis. Definitive diagnosis can be difficult as many other skin conditions can resemble atopic dermatitis. Therefore, diagnosis relies on the clinical history, exclusion of other conditions, such as flea allergy dermatitis and infection, and the clinical presentation at the time of examination.

The predominant breeds of dog used by the Guide Dogs for the Blind Association (GDBA) in the UK are the Labrador retriever, golden retriever and their crosses. Both of these breeds are susceptible to the development of atopic dermatitis. Most GDBA dogs undergo training and begin their working career between one and two years of age. As most dogs develop clinical signs of atopic dermatitis between one and three years of age, this means that valuable resources are often expended on dogs which may not be able to work to their full ability because they suffer from atopic dermatitis.

The aim of this study was to develop a predictive model that could be used within the GDBA training centres, to identify individual dogs at risk of developing atopic dermatitis before chronic skin complaints were evident.

As part of this model, we hoped to identify whether or not there were any significant differences between atopic and non-atopic dogs in the age at which they first developed skin disease, and in the frequency of episodes of skin disease.

MATERIALS AND METHODS

Clinical histories of 30 dogs from the GDBA were examined. Fifteen of these dogs had previously been diagnosed as atopic, based on clinical findings, the exclusion of other skin conditions and at least one positive result on intradermal skin testing. At the time of the study, these dogs ranged in age from two to 11 years.

Fifteen non-atopic dogs were chosen at random by the Kennel Assistants at the

GDBA based on the criteria that all dogs were older than four years of age by the time of the study and that there were no skin problems suggestive of atopic dermatitis in the clinical history. Although otitis externa and pyoderma are included in Willemse's criteria (Willemse 1986) as clinical signs of atopic dermatitis, dogs were only excluded if they had a history of repeated episodes of these conditions as non-atopic dogs can have isolated cases of otitis externa. An age limit of four years rather than three years was chosen to ensure that the chance of these dogs still developing atopic dermatitis was minimised, although it is recognised that it is possible for a dog to develop atopic dermatitis after four years of age. Willemse and Van den Brom (1983) reported that 75.5 per cent of cases of atopic dermatitis developed before three years of age. The non-atopic dogs chosen were aged between four and 11 years.

All 30 dogs were either golden retrievers, Labrador retrievers or crosses of these two breeds. Detailed clinical histories were available for all of the dogs from birth to 21 months of age.

Clinical histories were examined for mention of any skin problems, excluding viral papillomas and pressure sores. As these conditions were not consistently present throughout the time being studied, it was not felt appropriate to include them. Atopic-type skin conditions were based on the criteria of Willemse (1986) and included pruritus, otitis externa, conjunctivitis, pedal dermatitis, pyoderma, erythema, dandruff and anal gland disease.

"Any skin condition" describes atopic-type conditions in addition to skin problems such as alopecia and wounds but does not include viral papillomas or pressure sores.

Age at presentation

The age at which dogs first presented with any skin condition or an atopic-type skin problem was recorded and an event curve of time to event produced for both of these findings. Atopic and non-atopic dogs were compared for any significant differences in the age at which they first presented with atopic-type or any skin conditions using a Kolmogorov-Smirnov two-sample statistical test.

Duration of clinical signs

To facilitate statistical analysis, the average length of time, which a particular skin condition took to resolve, had to be determined. This was defined in non-atopic dogs as the length of time between first being examined by the training centre vet until complete resolution of the problem. Only conjunctivitis, otitis externa, pedal dermatitis and acute moist dermatitis/pyoderma were observed often enough to allow statistical evaluations to be carried out. Acute moist dermatitis and pyoderma were both used by the training centre vet to describe bacterial skin disease and could not be differentiated on the clinical records – therefore, both conditions had to be included as one. Statistical analysis of these results was carried out to obtain a 90 per cent non-parametric confidence interval for the median times to resolution to define the expected duration of each skin condition.

Frequency of presentation

The frequency with which atopic dogs presented with the conditions listed above was examined retrospectively. Using the median times to resolution in non-atopic dogs as a guide, the number of episodes of each skin condition was calculated for each individual. Where an episode of skin disease in an atopic dog lasted twice as long as that expected in a non-atopic dog, the atopic dog was described as being affected by two episodes of skin problems. This was necessary because atopic dogs can suffer from prolonged episodes of skin disease, which do not respond quickly to treatment and this fact has to be taken into account when comparing both groups of dogs.

The cumulative number of episodes of particular skin conditions in atopic and non-atopic dogs, at various ages, were analysed using a Mann-Whitney statistical test. This allowed the identification of the most significant diagnostic parameters. Analyses were undertaken using the Minitab version 11.21 (1996) statistical software package.

To use the above information as part of a predictive model, sensitivity, specificity and predictive values were examined to identify the clinical parameters best suited as a diagnostic indicator for the development of atopic dermatitis later in life.

Sensitivity was defined as the number of atopic dogs in the study which agreed with the criteria of x number of episodes by y months of age, and specificity was defined as the number of non-atopic dogs in the study which were not affected by x number of episodes by y months of age. Or in simpler terms, sensitivity was the number of true-positive results (atopics) and specificity the number of true-negative results (non-atopics). So, for example, if all atopic dogs had three cases of conjunctivitis by the age of nine months but none of the non-atopic dogs did, then this would give a sensitivity of 100 per cent and a specificity of 100 per cent.

Predictive value was calculated using a prevalence of 10 per cent combined with the calculated sensitivity/specificity results according to the following equation:

$$\text{Predictive value} = \frac{\text{Prevalence} \times \text{Sensitivity}}{(\text{Prevalence} \times \text{Sensitivity}) + [(1 - \text{Prevalence}) \times (1 - \text{Specificity})]}$$

RESULTS

Studies of the skin conditions in atopic and non-atopic dogs showed that otitis externa was the most common condition in both atopic and non-atopic dogs followed by conjunctivitis. Conditions other than atopic-type skin conditions observed in both atopic and non-atopic dogs included juvenile cellulitis, wounds, alopecia, lick granulomas and infected nail beds.

Examination of the age at which dogs first showed any kind of skin condition (Fig 1), excluding viral papillomas and pressure sores, revealed that nine of 15 of the atopic dogs had showed skin problems by the age of seven months compared with only three of 15 non-atopic dogs.

All 15 atopic dogs had suffered from some form of skin condition by 11 months of age and atopic-type skin conditions by 15 months of age (Fig 2) compared with 22 months of age for the development of both atopic and any kind of skin condition in all 15 non-atopic dogs.

Event curve analyses of the number of atopic and non-atopic dogs affected by skin problems by particular ages showed

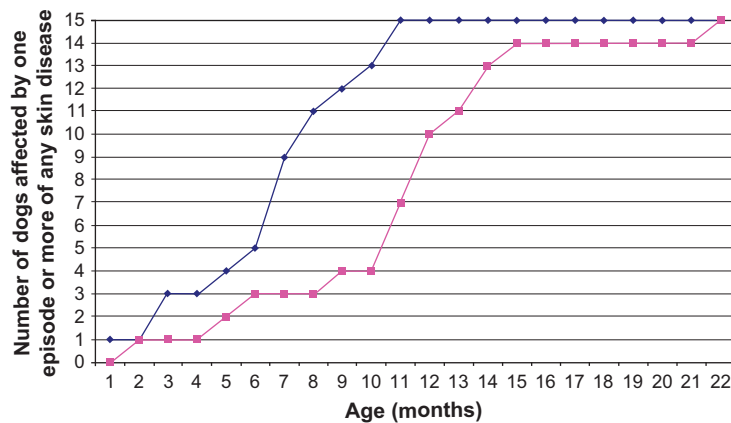


FIG 1. Event curve of the time to the development of any skin disease for atopic and non-atopic dogs

that atopic dogs were consistently affected by skin disease at a younger age than the non-atopic dogs.

Comparison of the event curves of atopic and non-atopic dogs with a Kolmogorov-Smirnov test (Siegel and Castellan 1988) showed a significant difference between both groups of dogs at 10 months of age for any skin conditions ($P<0.01$) and atopic-type skin conditions ($P<0.02$).

Examination of the length of an episode of atopic-type skin conditions in non-atopic dogs showed the estimated expected duration of each particular skin condition to be seven days for conjunctivitis, otitis externa and pedal dermatitis and 14 days for pyoderma.

Examination of the cumulative number of episodes of skin disease in atopic and non-atopic dogs at differing ages was carried out using a Mann-Whitney test. This

showed a significant difference between atopics and non-atopics at nine months for the total number of episodes of both atopic-type skin conditions ($P<0.025$) and any skin conditions ($P<0.042$). No significant difference was evident until 12 months between atopics and non-atopic for otitis externa ($P<0.002$) and 18 months for conjunctivitis ($P<0.02$). No difference was observed between the two groups in the number of episodes of pedal dermatitis or pyoderma.

Examination of the number of episodes of each condition at various ages in atopic and non-atopic dogs showed the best predictive value for four or more episodes of atopic-type skin conditions by the age of 15 months. This gave a sensitivity (correct identification of atopic dogs) of 60 per cent and a specificity (correct identification of non-atopic dogs) of 93.3 per cent.

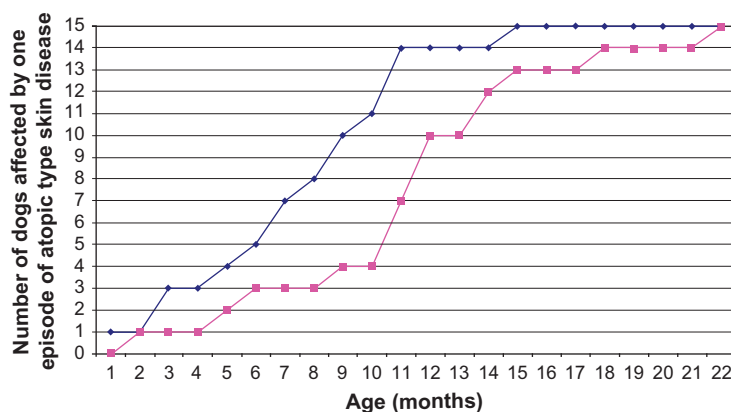


FIG 2. Event curve of time to the development of atopic-type skin disease for atopic and non-atopic dogs

DISCUSSION

Atopic dermatitis is characterised as a pruritic skin condition, which is often familial and generally affects particular breeds (Scott 1981, Willemse 1986). All 30 dogs in this particular study were golden retrievers, Labrador retrievers and their crosses which are breeds known to be predisposed to developing atopic dermatitis (Willemse 1986).

Most cases of atopic dermatitis become clinically evident between the ages of one and three years (Scott 1981, Zur and others 2002). However, clinical signs of skin problems can present before this age, but as they are often minor they may not be regarded as significant by an owner. The clinical histories of the working dogs in this study are highly detailed and in this respect minor skin conditions which may not be observed in pet dogs have been recorded.

Diagnosis of atopic dermatitis before one year of age is difficult as diagnosis often relies on a history of chronic relapsing skin problems. Willemse and Van den Brom (1983) observed that only 27 per cent of atopic dogs had developed clinical signs of atopic dermatitis by one year of age, whereas Scott (1981) found that 64 per cent of atopic dogs had developed signs by one year of age.

Examination of the clinical histories of the working dogs described here showed that there was indeed a significant difference between atopic and non-atopic dogs in the age at which dogs first showed skin problems. This difference was evident by 10 months of age. Examination of both atopic-type skin conditions and any skin conditions showed that the atopic dogs first showed such skin problems at a significantly younger age than the non-atopic dogs.

The age at which dogs first show skin problems can therefore be included in the diagnostic criteria of atopic dermatitis, and examination of a dog's history is important in the diagnosis of atopic dermatitis. However, these episodes of skin disease may be so minor that owners of pet dogs may fail to recognise them. However, this should not be a problem in the GDBA population where puppy walkers could be informed of the clinical signs to look for.

Evidence of pruritus is the most common presenting clinical sign in canine atopic dermatitis (Scott 1981). However, it can be difficult to assess as it is subjective in nature and relies on the opinion of the owner. As it is normal for all dogs to show a degree of pruritus, diagnosis can prove difficult. In the kennels, working/training dogs are not observed at all times and pruritus may not be diagnosed unless it is very obvious. Therefore, pruritus is not mentioned regularly in the clinical histories and it could not be included as a major sign in this study.

The most commonly mentioned skin problems were conjunctivitis, otitis externa, pyoderma and pedal dermatitis, and separate statistical analysis of these parameters was possible. Other conditions such as anal gland disease were too infrequent to include in statistical analysis and each mention of these conditions was included as an episode of disease.

In the diagnosis of atopic dermatitis, the initial presentation of skin disease alone is not sufficient to make a diagnosis. Instead, diagnosis requires repeated episodes of skin disease, which obviously take time to become apparent. In addition, these repeated episodes of skin disease in both human beings and dogs can become chronic with each episode, taking a long time to resolve. It was therefore necessary to determine the expected duration of atopic-type skin conditions in non-atopic dogs. The expected duration of otitis externa in non-atopic dogs was found to be only seven days which is rather low as usually cases of otitis externa in GDBA dogs would be treated for a minimum of 14 days. It has been noted that individual dogs with large amounts of wax have been referred to the training centre veterinary surgeon as otitis externa and such cases are often recorded as otitis externa. These had to be included in this study as it was not possible to differentiate them from true cases of otitis externa. Similarly, cases of pedal dermatitis on average lasted for seven days, which again appears a rather short time. It is possible that these cases were because of trauma as many dogs tend to jump up onto the wire mesh kennel doors. However, such cases are equally represented in atopic and non-atopic populations and it is fair to include them in this study.

Comparison of atopic and non-atopic dogs showed that there was indeed a significant difference between the groups in the number of episodes of both atopic-type skin lesions and any skin lesions as early as nine months of age. This is younger than would be expected as most diagnoses of atopic dermatitis are not made before one year of age. However, it is likely that most atopic dogs do indeed begin to show clinical signs of disease at this young age but that the process of diagnosis often involving relapsing skin conditions means that the recorded age of presentation is older.

Of the individual skin conditions described, a significant difference was noted between the number of episodes of otitis externa experienced by atopics and non-atopics by the age of 12 months ($P < 0.002$). A significant difference was found for the number of episodes of conjunctivitis by 18 months of age ($P < 0.02$). There was no significant difference between atopic and non-atopic dogs in the number of episodes of pedal dermatitis or pyoderma. Comparison of atopic and non-atopic dogs showed a significant difference in the total number of episodes of atopic-type skin disease or any skin disease at nine months of age ($P < 0.025$ and $P < 0.042$, respectively). From this it appears that for diagnostic purposes, it is better to examine the total number of episodes of atopic-type skin conditions or indeed any skin conditions rather than relying on one particular skin condition.

The finding that atopic dogs as young as nine months of age have significantly more episodes of skin disease than non-atopics contradicts work by Schwartzman (1984) who could not find any clinical evidence of atopic dermatitis in dogs less than 12 months of age. However, the work described in the present study could not detect atopic dermatitis in dogs as young as those studied by Reedy and others (1997), who observed that dogs could show clinical signs consistent with a diagnosis of atopic dermatitis by the time they were six months of age. In order for such an observation to withstand statistical scrutiny, increased numbers of dogs would have to be studied.

A range of values for the prevalence of atopic dermatitis in the general population have been put forward by Hillier and

Griffin (2001) ranging from 3 to 15 per cent, although these authors concluded that the true prevalence was unknown. For the purposes of this study, a prevalence of 10 per cent was used for statistical evaluation.

Retrospective examination of clinical findings showed a significant difference in the number of episodes of atopic-type skin disease or the number of episodes of any skin disease between atopic and non-atopic dogs by nine months of age. However, to apply these data in the prediction of atopic dermatitis, dogs that show four or more episodes of atopic-type skin disease by the age of 15 months should be considered at risk of developing atopic dermatitis. Sensitivity of this finding was 60 per cent and specificity 93 per cent. Although the sensitivity is lower than desired, the high specificity means that there would be a low chance of non-atopic dogs being identified as possible atopics. This would allow dogs to be assessed at the beginning of their training and a decision could be made about their future before they go through two years of training.

It is concluded that atopic dogs within the GDBA population show clinical evidence of skin problems both of an atopic and non-atopic nature at a younger age than non-atopic dogs. It is therefore important that the clinical history of a suspected atopic dog is examined in some detail and that the age at which dermatological disease of any sort was first recognised is included in the diagnostic parameters of canine atopic dermatitis.

In addition, examination of the cumulative number of episodes of atopic-type skin conditions or any skin problems are a better diagnostic indicator than episodes of any one particular form of skin disease. Analysis of the number of episodes of skin problems should therefore be carried out in suspected atopic dogs. Those animals affected by four or more episodes of skin disease by the age of 15 months should be investigated further as candidates for the development of atopic dermatitis.

While it is appreciated that these findings are specific for the GDBA population owing to their detailed and consistent historical clinical information, it would be of interest to design a prospective study applied to the general pet dog population for comparative purposes.

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