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Does exposure to cats and dogs decrease the risk of developing allergic sensitization and disease?

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Sensitization to domestic pets, particularly cats and dogs, is an important risk factor for allergic diseases, such as asthma and allergic rhinitis.¹ Although cat and dog allergens are known asthma triggers and can influence disease severity among sensitized individuals,² their role in the development of sensitization and allergic disease is less clear and has remained a subject of debate. Recent studies suggest that pet exposure, particularly in early childhood, may have beneficial effects and may actually prevent the development of atopic disorders.³ In this issue of the *Journal*, the longitudinal investigation by Mandhane and coworkers provides further evidence that exposure to the most common pets, cats and dogs, lowers the risk of developing allergic sensitization, not only in children but also in young adults.⁴

Over the past decades, numerous studies have investigated the role of pet exposures in relation to atopy, but the published findings have been inconsistent and sometimes conflicting.^{1, 3} Although there is growing evidence that exposure to pets may protect against development of atopic outcomes, the protective effects have not been replicated in all studies. On the other hand, this is not necessarily surprising, because there might be multiple factors that contribute to the inconsistencies, including differences in study design and population characteristics (e.g., age, atopic history, prevalence of pets in the community), as well as timing, duration, and intensity of exposures.

Although the complex relationships between pet exposures and development of allergic sensitization and disease are not completely understood, potential biological mechanisms that may underlie the protective effect of pets have been proposed. Substantial evidence has emerged to support the view that high-dose exposure to cat allergen can induce an immune-response (modified Th2 response) which is non-allergic in nature.⁵ Alternatively, it has been hypothesized that exposure to microbial products, specifically endotoxin, can affect the balance between Th1 and Th2 responses, shifting it away from Th2-type responses.⁶ Further research, however, is needed to clarify the mechanisms that contribute to the protective effect of pets; without understanding the mechanisms, it will be difficult to develop approaches to prevent atopic outcomes.

Most epidemiological studies investigating pet exposures in relation to atopic outcomes have focused on childhood. The study of Mandhane et al. extends the time window to adulthood,⁴ providing a unique opportunity to examine whether or not exposures to cats and/or dogs

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contribute to the development of atopy over time. Indeed, an important strength of this study is that the data comes from a large, unselected, population-based birth cohort with an impressive length of follow-up (32 years) and an excellent retention rate. The study showed that living with cats and dogs was associated with a lower risk of developing atopy during childhood and young adulthood. Among adults, parental history of atopy appeared to modify the association. Interestingly, the observed protective effect of pet ownership was seen only in subjects who had had both types of animals at home. Moreover, the reduction in risk of sensitization applied to both indoor and outdoor allergens. Although an inverse association, such as that demonstrated here, could result from selective avoidance of pets, the authors did not find any evidence of selection bias. Pet ownership in the study population was not influenced by parental history of atopy or development of atopy in the subjects. However, avoidance of pets in households who have asthmatic or allergic family members has been reported in several other studies.^{7, 8}

Unfortunately, the findings of Mandhane et al. may not be generalizable to other populations with lower rates of pet ownership. In this population, pet ownership was extremely common; of the study participants, the vast majority (87.6%) had owned a cat or a dog by age of 9 years, and the prevalence of pet ownership was even higher later in life.⁴ In the United States, as well as in many European countries, pet ownership is substantially lower. In a nationally representative sample of US households, less than half (45.1%) of the households had either dog(s) or cat(s) present in the home.⁹ A recent multicenter study suggested that cat ownership in Europe is highly variable, but not exceptionally high; prevalence of ownership ranged from 2.4% (Spain) to 36.6% (UK).¹⁰ Because of passive transport of cat and dog allergens, the community prevalence of cat and dog ownership has been shown to influence pet allergen levels in non-pet owners' homes and other environments where no cats or dogs are present (e.g., schools and daycares).¹⁰⁻¹² There is evidence that the community exposure to pets may also affect the risk of developing atopic outcomes.^{1, 13} Mandhane and coworkers did not measure allergen levels in their study, but used cat and dog ownership as a proxy of exposure.⁴ Without objective measurements, it is not possible to evaluate whether the protective effect was associated with cat and/or dog allergens or with other exposures, such as endotoxin and other microbial products that have been linked to the presence of animals. As the number of pets was not recorded, it remains unknown whether the cumulative exposure, not necessarily the diversity of pets, conferred the protection against sensitization.

Although several studies have reported protective effects of pet exposures on asthma and wheezing, the findings have been inconsistent, even in longitudinal studies.³ Recently, a Dutch birth cohort study reported that early presence of pets provided protection against the subsequent development of sensitization to inhalant allergens, but it did not prevent subsequent development of asthma.¹⁴ The study of Mandhane et al. did not examine pet exposures in relation to the development of asthma.⁴ It is well known, however, that New Zealand has one of the highest asthma prevalence rates in the world.^{15, 16}

Our understanding of atopic illness has improved in recent years, but many questions still remain. As the onset of sensitization and allergic disease is likely a function of intensity, duration and timing of exposure(s), longitudinal studies will provide the most reliable information on whether exposures, such as the presence of cats and dogs, increase the risk of sensitization and allergic disease or protect against the development of atopic outcomes. It would be tempting to test the influence of pet ownership and atopic heredity in a randomized controlled trial, but practical and ethical concerns make this impossible. To achieve a better understanding of the role of environmental factors, including cat and dog exposures, in the development of atopy, more standardized and validated exposure assessment methods are needed in the future. Objective exposure assessment is crucial in order to elucidate potential mechanisms that contribute to the observed effects. It is not always possible to collect

information prospectively, but retrospectively collected information may be an important source of recall bias. For example, in a recent study, 40% of the parents who reported physician-diagnosed asthma in data that was collected prospectively, said retrospectively that a physician never diagnosed their child with asthma.¹⁴ Further research focusing on genetic susceptibility and interactions between environmental and genetic factors is important because potential interactive mechanisms may modify the risk of atopic disease. There are data emerging that exposure to a specific environmental agent (e.g., endotoxin) can have different effects in individuals with different genotypes.^{17, 18}

Despite increasing evidence that pets provide psychosocial and other possible health benefits to their owners, further studies, mechanistic and epidemiological, are warranted to address the gaps in the research. It is not yet known whether, and to whom, clinicians should recommend cat and dog ownership as a preventive measure for development of atopy.

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