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The Effect of Early Diet on Canine Atopic Dermatitis (CAD) in Three High-Risk Breeds

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Abstract: The effect of diet on the occurrence of canine atopic dermatitis (CAD) in the high-risk breeds boxer, English bull terrier and West Highland white terrier was investigated as part of an extensive case-control study. In that study, a sparing association was seen for feeding the bitch a diet containing non-commercial ingredients during lactation and the subsequent development of CAD in the offspring. The purpose of this study was to further explore the role of diet of the bitch during lactation as well as early dietary exposure of puppies (up to six months of age) on the occurrence of CAD.

Two factors were significant in a final logistic regression model: "not feeding non-commercial animal products (meat, egg or milk-products) to the bitch during lactation" (OR = 3.39, 95% CI 1.46-7.92) and "feeding non-commercial meat to the puppy between the age of 2-6 months" (OR = 2.97, 95% CI 1.27-6.93), and further analysis revealed that there was an interaction between these two factors.

If a bitch didn't receive non-commercial animal products during lactation, and the puppy was fed non-commercial meat any time until 6 months of age, the puppy had an increased risk of developing CAD (OR = 5.1, 95% CI 1.2-21.9). If the bitch received at least some non-commercial animal products during lactation there was no difference in risk of CAD for the offspring, regardless of whether the puppy was fed non-commercial meat or not until the age of 6 months (OR = 1.6, 95% CI 0.5-5.6). It seems prudent to feed bitches some non-commercial animal products during lactation.

INTRODUCTION

Canine atopic dermatitis (CAD) is defined as a genetically predisposed inflammatory and pruritic allergic skin disease with characteristic clinical features. It is most commonly associated with IgE antibodies to allergens in the environment [1]. Common clinical signs of CAD are pruritus, particularly affecting the face, ears, paws, extremities, and/or ventrum. The typical age of onset of CAD is before three years of age [2].

In a recent Swedish epidemiological study we have estimated that the incidence of the disease was 1.7 cases per 1000 dog-years at risk in a population of 220,496 insured dogs. To belong to a high-risk breed increased the risk for CAD as did living in a city, in the south or central parts of the country, or to be born in the autumn [3]. The risk of CAD was further shown to increase with increasing annual rainfall, human population density and among dogs living in the same county as a veterinary dermatologist [4].

In industrialized countries, human atopic dermatitis has increased during the last decades, and known risk factors are early diet, allergens, tobacco smoke, infections and pollutants [5]. Sugiyama *et al.* [6] found that if the mother of a child had atopic dermatitis, this increased the risk for atopic dermatitis during the first year of life for the child. Perkin & Strachan [7] showed a lower prevalence of AD in children exposed to unpasteurized milk compared to those that consumed pasteurized milk.

In our recently published case-control study of general risk factors of CAD in three high-risk dog breeds, feeding a diet including non-commercial ingredients to the bitch during lactation had a protective effect on the development of CAD in the offspring. The odds of developing CAD were twice as high in the offspring from bitches that were not exposed to home-made/non-commercial diets (OR 2.0, 95% CI 1.2-3.8) [8]. This generated the hypothesis that microbial exposure in early life by being exposed to "non-commercial dietary constituents" might stimulate the development of the immune-system in a way that provides protection against allergies. As many dogs and humans share the part of the diet given by table foods, and also share the same environment in other regards, we believe that these results might also be interesting for humans.

The main aim of this study was to further explore the relationship between dietary exposure and the development of CAD, specifically to determine if there were differences in the types of non-commercial ingredients consumed by cases or controls before the age of six months or by their mothers during pregnancy and lactation. An additional objective was to describe the diets fed to this sample of dogs and their mothers in detail, and to explore if there were any interactions between the different exposures.

MATERIALS AND METHODOLOGY

Cases and controls. As described in more detail elsewhere [9] cases and controls were selected in three high-risk breeds for CAD in Sweden; English bullterrier, West

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Highland white terrier and boxer. The CAD cases were recruited prospectively by twelve Swedish veterinarians with a special interest in dermatology. The cases were diagnosed using criteria modified from Willemse [8, 9]. The dogs were classified as having CAD if they fulfilled the inclusion criteria after exclusion of ectoparasites, skin infections (bacterial pyoderma or *Malassezia* dermatitis), and if the dogs had a negative response to strict elimination diets (novel or hydrolysed protein) for 8 weeks. However, previously diagnosed cases were also included as CAD cases if a minimum of 50% improvement in clinical signs had been recorded on treatment with immunotherapy, even if a dietary trial had not been performed. All cases had demonstrated presence of allergen-specific IgE by the use of intradermal test or allergen-specific IgE serology test (ALLERCEPT® Definite Antigen Panels, Heska AG; Fribourg, Switzerland).

Cases were matched to controls of the same breed and year of birth, randomly selected among registered dogs at the Swedish Kennel Club registry [10]. To allow for possible non-responders, four controls per case were initially selected, and the selection of controls was made when a new case was identified continuously during the study period. Most controls visited one of the twelve specialized veterinarians recruited to this project, but if that was impossible a visit to another veterinarian was organized. Dogs were excluded from the control group if they had clinical signs of CAD, or if they had previously had a history of pruritus, otitis externa and/or interdigital dermatitis. If the controls were younger than three years of age, a follow-up call was made after the dog had become three years of age, to ensure that it had not developed any of the above mentioned clinical signs. The protocol was approved by the appropriate animal research ethical committee. The study was performed during the years 2003 - 2005.

Data Collection. The owners of cases and controls were asked to complete an owner questionnaire when visiting the veterinarian. This questionnaire included data on demographics as well as environmental exposure including dietary intake of the dogs when they were between 2-6 months of age. It was recorded whether the dog consumed dry or canned dog food, table foods or home-made diets as well as any vitamin- and mineral supplements or treats. It was also registered what commercial or home-made product/ingredient were consumed, in what frequency, and what amount. The majority of the questions were of multiple-choice type.

Breeders of cases and controls were contacted after permission from the owners of dogs included in the study. A combined mail and telephone questionnaire was posted (after the validated dietary questionnaire by Sallander *et al.* [11]), where the breeders were asked to fill in the questionnaires prior to the interview to make it as efficient as possible and to avoid difficulties and ambiguities when analysing the questionnaire answers. The second author, who was trained in interviewing techniques, performed the interviews within a few weeks from the distribution of the posted questionnaire. The interviews took about 10-30 minutes to complete for each individual. The non-responders who were difficult to get hold of by telephone were contacted at least five times at different times of the day and also received the questionnaire by mail once again before they were deemed non-contactable.

The questionnaire sent to the breeders contained questions about diet and feeding of the bitch during pregnancy and lactation, and the diet of the puppy during its first 2 months. It was recorded whether the bitch consumed dry or canned dog food, table foods or home-made diets, vitamin- and mineral supplements or treats as well as what specific commercial or home-made product/ingredients were consumed, in what frequency and amount. It was noted at what age the puppy was introduced to solid food and when weaning was started and completed as well as what ingredients were fed at those times. The majority of the questions were of multiple-choice type.

Analysis. In the calculations it was decided to combine the two variables table foods and home-made diets as one variable as these two included the same types of non-commercial ingredients.

All continuous outcome variables were initially tested against case status using 2-sample t-tests, while categorical outcome variables were tested with the Pearson chi-squared statistic. All variables were initially screened, keeping a liberal p-value of less than 0.25, while the traditional p-value ($p<0.05$) was used as a cut-off limit in the final logistic regression model.

Before entering all variables with a p-value of less than 0.25 into a final logistic regression model, the colinearity was checked by a correlation matrix, and if the correlation was ≥ 0.7 ($p<0.05$), the variable with the weakest association to case status was omitted from further analysis. A backward manual elimination regression process was made ($p<0.05$), and significant variables were checked for interaction. The goodness-of-fit of the model was assessed based on Pearson, Deviance and Hosmer-Lemeshow tests. The data were analysed using Minitab Statistical Package [12].

The interaction between the two variables found significant in the logistic regression analysis was analysed in EpiInfo [13] using the Mantel-Haenszel chi-square and exact confidence intervals.

RESULTS

Demographic data. Owners of 65 cases and 61 controls completed the owner questionnaire handed out at the veterinary visits (n = 126). As a few of the owners did not allow us to contact their breeder, a breeder questionnaire was sent to breeders of 55 cases and 60 controls (n = 115). The overall response of the breeders was 92% (106/115), and the response of the 75 breeders possible to contact was 98% (106/108). The reasons why dog breeders did not participate were in descending order that the persons were not possible to contact because they did not answer the phone during the study (n = 5), incorrect addresses/phone numbers (n = 3), and that they did not want to participate (n = 1).

Twenty-three breeders had more than one dog included in the study; either only in the case group (three breeders with two dogs each), only in the control group (three breeders with two dogs each, and one breeder with three dogs), or in both groups (nine breeders with one case/one control, two breeders with two cases/one control, three breeders with one case/two controls, one breeder with one case/three controls, one breeder with three cases/one control). This proportion of breeders included 56 dogs in total. The distribution of breeds and gender of included cases and controls is presented in Table **1**. The dogs were born between 1994 and 2004 (median age 6.0 years, range 1-11).

Table 1. The Distribution of Breeds and Gender of Included Cases and Controls in a Study Performed with Owner (n = 126) and Breeder (n = 106) Questionnaires on Risk Factors for CAD

Variable	Breeder Questionnaire		Owner Questionnaire	
	Cases *(n = 51)*	Controls *(n = 55)*	Cases *(n = 65)*	Controls *(n = 61)*
Breed				
Boxer	25	24	32	25
Bullterrier	5	5	8	6
West Highland white terrier	21	26	25	30
Gender				
Female	26	28	37	31
Male	25	27	28	30

Diet and feeding patterns of the bitches during pregnancy and lactation. The majority of the bitches consumed dry dog food, and it constituted the main food source during pregnancy and lactation, as this was given frequently and in larger amounts compared to other ingredients (Table **2**). Mothers of cases and controls consumed similar types of dry dog foods during pregnancy (33 and 42% consumed a puppy/performance type of diet, 44 and 43% an adult type, and 23 and 21% were fed both of these types of commercial diets, respectively). During lactation there was also a similar pattern of exposure between cases and controls (60 and 56% consumed puppy/performance dry foods, 31 and 36% adult foods, and 4 and 4% were given both of these types of dry foods, respectively). One variable was significant at the liberal $P<0.25$ level: "feeding dry foods to the bitch during pregnancy, yes/no", and one variable at the $P<0.01$ level: "feeding only commercial foods during lactation to the bitch" (Table **2**).

There was no significant difference in the consumption of table foods/home-made diets between mothers of cases and controls during pregnancy. For lactation, one variable was significant at the $P<0.01$ level: "feeding table foods/home-made diets to the bitch during lactation, yes/no" (Table **2**). Also, three food ingredient variables were considered significant at the liberal $P<0.25$ level: "feeding non-commercial meat to the bitch during lactation, yes/no", "feeding non-commercial egg to the bitch during lactation, yes/no", "feeding non-commercial milk products to the bitch during lactation, yes/no"; Table **3**).

Both during pregnancy and lactation, vitamin- and mineral supplements as well as treats were served to a similar proportion of mothers (bitches) of cases and controls (Table **2**). Among bitches that were fed supplements, multivitamin- and minerals were given to 33% of the cases and 34% of the controls. Single vitamin supplements were given to 29% of the cases and to 34% of the control dogs. Fatty acid supplements were given to few individuals (4 and 11% of the cases and controls, respectively, which was not a significant difference). One variable was significant at the liberal $P<0.25$ level: "feeding treats to the bitch during pregnancy, times/day".

Diet and feeding patterns of the early puppy diet (weaning-2 months of age). The case and control puppies were of the same age (median 3.0 weeks; range 0-6 weeks) when the first food, other than the mother's milk, was introduced. Neither was there any significant difference in the age when the puppies were totally weaned (median 7.0 and 6.7 weeks for cases and controls, respectively), although there was a large variation in individual weaning age (2-10 weeks for cases, and 4-8 weeks for controls).

The majority of puppies were served home-made diets as their first solid meal, and there was no difference between the cases and controls (Table **2**). The most commonly given ingredients in the first meals were minced beef, egg, and corn gruel (Table **3**).

The majority of puppies consumed dry dog food after being weaned, and this constituted the main part of the diet. Dry foods were given more often and in larger amounts compared to other ingredients in the diet (Table **2**). Commercial products intended for this life-stage were the most popular, and puppy dry food was given to 86 and 91% of the cases and controls, respectively.

During the period from weaning to two months of age, both cases and controls were given table foods/home-made diets with ingredients mainly from sour milk, corn gruel, meat, and egg. One ingredient was significantly associated with case status at the $P<0.05$ level: "feeding non-commercial vegetable oil to the puppy between weaning-2months of age, yes/no". Two variables were significant on the $P<0.25$ level: "feeding non-commercial grains to the puppy between weaning-2months of age, yes/no" and "feeding non-commercial vegetables to the puppy between weaning-2months of age, yes/no" (Table **3**).

Two variables concerning vitamin and mineral supplements were significant at the $P<0.25$ level:"feeding vitamin/mineral supplements to the puppy between weaning-2 months of age, yes/no" and "feeding vitamin/mineral supplements to the puppy between weaning-2 months of age, times/day" (Table **2**). Of the individuals fed supplements, 6% of the cases and 13% of controls were fed multivitamin- and mineral supplements, and 6% of cases and 9% of controls were given single vitamin supplements; these differences were not significant.

Diet and feeding patterns during the later puppy period (2-6 months). Six dietary variables concerning the puppy diet during 2-6 months of age were significantly associated with case status at the $P<0.25$ level: "feeding dry food to the puppy at 2-6 months of age, yes/no", "feeding dry food to the puppy at 2-6 months of age, times/day", "feeding canned food to the puppy at 2-6 months of age, yes/no", "feeding table foods/home-made diets to the puppy at 2-6 months of age, yes/no", "feeding treats to puppies at 2-6 months of age, yes/no" and "feeding treats to puppies at 2-6 months of age, times/day" (Table **4**).

Table 2. Dietary Questions from the Breeder Questionnaire in a Case-Control Study of CAD in Boxers, English Bullterriers and West Highland White Terriers in Sweden (n = 106)

Food Item	Cases (n = 51)			Controls (n = 55)		
	Yes %[2]	Frequency Times/Day[3]	Total Amount Consumed Per Day (dl DM; Mean)[1, 3]	Yes %[2]	Frequency (Times/Day)[3]	Total Amount Consumed Per Day (dl DM; Mean)[1,3]
Feeding of the *bitch during pregnancy*						
Ad libitum feeding	28	-		31	-	
Dry food	88	2.4	7.27	95*	2.3	6.49
Canned food	10	2.4	1.32	9	1.7	0.68
Only commercial food	41			36		
Table foods/ home-made diets	59	1.6	0.46	64	1.9	0.91
Vitamin/ mineral supplements	31	0.9	-	32	1.1	-
Treats	18	0.9	0.57	27	1.4*	0.88
Feeding of the *bitch during lactation*						
Ad libitum feeding	44	-	-	36	-	-
Dry food	92	2.8	8.40	95	2.8	8.37
Canned food	8	2.7	2.16	7	2.7	2.16
Only commercial foods	51			29**		
Table foods/ home-made diets	53	1.7	0.39	71**	2.0	0.58
Vitamin/ mineral supplements	32	1.0	-	40	1.0	-
Treats	12	0.9	0.60	20	0.9	0.49
The first food of the *puppy during weaning*						
Dry food	16	-	-	18	-	-
Canned food	6	-	-	7	-	-
Only commercial food Table foods/ home-made diets	14 86	-	-	13 87	-	-
Feeding of the *puppy between weaning and normal age for delivery (2 months of age)*						
Ad libitum feeding	20	-	-	18	-	-
Dry food	94	3.7	3.37	91	3.8	4.22
Canned food	6	4.0	0.52	5	4.0	0.52
Only commercial food	27			22		
Table foods/ home-made diets	73	1.0	0.38	78	1.0	0.36
Vitamin/ mineral supplements	8	0.7	-	16*	1.3*	-
Treats	6	-	-	9	-	-

[1]To calculate the amount of feed given to each dog; the DM has been estimated to 90% in commercial dry dog foods, and to 20% in canned foods, table foods and home-made diets.
[2]chi-squared test sign at *p<0.25, **p<0.05.
[3] Two sample t-test sign at *p<0.25, **p<0.05.

Table 3. Table Foods and/or Home-Made Diets as Specified Ingredients in Diets Used to Bitches and Puppies – DATA from a Breeder Questionnaire in a Case-Control Study of CAD in Boxers, English Bullterriers and West Highland white Terriers in Sweden (n = 106)

Question[1]	Cases (n = 51)	Controls (n = 55)
	Yes %	*Yes %*
Feeding of the *bitch during pregnancy*		
Meat	45	44
Egg	12	13
Milk products	6	9
Grains (rice etc.)	18	15
Pasta	12	11
Vegetables	18	13
Vegetable oil	12	20
Corn gruel	2	4
Feeding of the *bitch during lactation*		
Meat*	37	51
Egg*	14	24
Milk products*	10	18
Grains (rice etc)	14	13
Pasta	12	13
Vegetables	18	16
Vegetable oil	12	16
Corn gruel	4	0
The first feed of the *puppy during weaning*		
Meat	63	67
Egg	37	40
Milk products (here only sour milk)	23	20
Grains (rice etc)	4	5
Pasta	0	0
Vegetables	0	2
Vegetable oil	0	2
Corn gruel	22	16
Feeding of the *puppy between weaning and normal age for delivery (2 months of age)*		
Meat (here only minced beef)	31	31
Egg	47	51
Milk products (mainly sour milk)	53	60
Grains (rice etc.)*	10	18
Pasta	10	7
Vegetables*	4	11
Vegetable oil**	4	16
Corn gruel	42	42

[1]Chi-squared test sign at *p<0.25, **p<0.05.

Also three ingredients were significant at the p<0.25 level: "feeding non-commercial pasta to the puppy at 2-6 months of age, yes/no", "feeding non-commercial vegetables to the puppy at 2-6 months of age, yes/no" and "feeding non-commercial vegetable oil to the puppy at 2-6 months of age, yes/no". One ingredient variable was significant to the case status at the P<0.01 level: "feeding non-commercial meat to the puppy at 2-6 months of age, yes/no" (Table **5**).

Out of the cases, 6% were given multivitamin- and mineral supplements, 8% single vitamin supplements, and 1% fatty acid supplements. Eight percent of the controls were fed multivitamin- and mineral supplements, and five percent were given single vitamin supplements, and there were no significant difference between cases and controls.

Logistic regression model. Variables that in the initial screening (Tables **2-5**) were associated with CAD were offered to the model, except "feeding non-commercial meat to the bitch during lactation, yes/no" which was removed due to high correlation to "feeding table foods/home-made diets to the bitch during lactation, yes/no" (r = 0.75), and "feeding table foods/home-made diets to the puppy at 2-6 months of age, yes/no" which was removed because of high correlation to "feeding non-commercial meat to the puppy at 2-6 months of age, yes/no" (r = 0.81). As an alternative to enter the non-commercial animal products meat, egg and milk as separate variables, a new variable was tested including all animal products (meat, egg *or* milk products) at each life stage. To produce a consistent direction of effect, the lactation variable was reversed to be "not feeding non-commercial animal products".

In the final logistic regression model there were two significant risk factors remaining; "not feeding non-commercial animal products (meat, egg or milk products) to the bitch during lactation" (OR = 3.39, 95% CI 1.46-7.92; P = 0.005) and "feeding non-commercial meat to the puppy between the age of 2-6 months" (OR = 2.97, 95% CI 1.27-6.93; P = 0.012). The goodness-of fit tests indicated that the model fit the data adequately.

To clarify the possible interaction between the two variables in the final model, a stratified Mantel-Haenszel analysis was done. A combined variable for whether the puppy was fed non-commercial meat anytime until the age of 6 months or not was made (the first food, weaning-2 months *or* 2-6 months). If a bitch did not receive non-commercial animal products during lactation, and the puppy was fed non-commercial meat any time until the age of 6 months of age, the puppy had an increased risk of developing CAD (OR = 5.1, 95% CI 1.2-21.9). Looking at bitches not consuming non-commercial *meat* during lactation instead of animal products, the trend is still the same, although the interaction is not quite significant at the 5% level (OR = 3.5, 95% CI 0.94-13.2; P = 0.06). If the bitch received at least some non-commercial animal products during lactation there was no difference in risk of CAD for the offspring, regardless of whether the puppy was fed non-commercial meat or not until the age of 6 months (OR = 1.6, 95% CI 0.5-5.6). There were 17 cases and 3 controls positive for the interaction (i.e. the bitch had not received non-commercial animal products and the puppy had received meat). All breeds were represented among both interaction-positive cases and controls, the controls were from three

Table 4. Dietary Questions from the Owner Questionnaire in a Case-Control Study of CAD in Boxers, English Bullterriers and West Highland White Terriers in Sweden (n = 126)

Food Item	*Cases (n = 65)*			*Controls (n = 61)*		
	Yes %[2]	Frequency *(Times/Day)*[3]	Total Amount Consumed Per Day *(dl DM; Mean)*[1, 3]	Yes %[2]	Frequency *(Times/Day)*[3]	Total Amount Consumed Per Day *(dl DM; Mean)*[1, 3]
Feeding *puppy 2-6 months of age*						
Dry food	82	2.5	7.00	74*	2.8*	6.72
Canned food	6	1.3	-	13*	1.4	0.64
Only commercial foods	45			54		
Home-made diets/ table foods	54	1.4	1.26	41*	2.0	1.8
Vitamin/ mineral supplements	16	1.4	-	18	1.2	-
Treats	51	1.3	-	39*	3.3*	-

[1]To calculated the amount of feed given to each dog; the DM has been estimated to 90% for commercial dog foods, and to 20% in canned foods, table foods and home-made diets.
[2]chi-squared test sign at *p<0.25.
[3] Two sample t-test.

different breeders; 12 breeders provided one case each; one breeder contributed two cases and one breeder three cases (this breeder also provided one positive control).

Table 5. Table Foods and/or Home-Made Diets as Specified Ingredients Used in the Owner Questionnaire in a Case-Control Study of CAD in Boxers, English Bullterriers and West Highland White Terriers in Sweden (n = 126)

Question[1]	Cases *(n = 65)*	Controls *(n = 61)*
	Yes %	*Yes %*
Feeding *puppy 2-6 months of age*		
Meat***	49	28
Egg	16	10
Milk products	16	13
Pasta*	25	15
Vegetables*	22	11
Vegetable oil*	16	8
Corn gruel	6	5

[1]chi-squared test sign at *p<0.25, ***p<0.01.

DISCUSSION

In the initial case-control analysis preceding this study, there was an indication of a protective effect on the development of CAD in her offspring by feeding a diet including non-commercial ingredients to the bitch during lactation [8]. In the present study, the dietary exposure was scrutinized in detail. The feeding variables were refined and it became clear that the effect was most pronounced for feeding of non-commercial animal products to the bitch during lactation rather than other table foods. Although the association for feeding non-commercial meat to the bitch was significant, the strongest association was for non-commercial animal products (meat, egg or milk products). When bitches had not received any non-commercial animal products during lactation, and then the puppy received meat until the age of 6 months, there was an increased risk for CAD later in life. If the bitch received animal products during lactation, the feeding of the puppy did not influence CAD risk. Based on these results it would seem prudent to feed bitches some non-commercial animal products, including meat during lactation. The results support the hypothesis that exposure to non sterile food constituents very early in life might protect from CAD.

Flohr *et al.* [14] made a meta-analysis of 64 relevant studies from 1966-2004 on AD in man, and generated the hypothesis that environmental microbial exposure early in life might stimulate the development of the immune-system in a way that provides protection against AD; the so called “hygiene hypothesis”. They also found that a few randomised controlled trials had suggested that probiotics (dietary supplements containing potentially beneficial bacteria or yeasts) could reduce AD severity and might also be able to prevent AD to some degree. Miraglia del Giudice & De Luca [15] performed a survey of the most relevant studies concerning the use of probiotics in human food allergy, atopic dermatitis, and in primary prevention of atopy. The authors showed that probiotics relieve allergic inflammation as measured by reduced clinical symptoms and a reduction of local and systemic inflammatory markers. Rautava *et al.* [16] conducted a study of 62 mother-infant pairs, and showed that if the pregnant and lactating mother was given probiotics, the immunoprotective potential of breast milk was increased, as evidenced by anti-inflammatory transforming growth factor beta2 (TGF-beta2) in the milk (2885 pg/mL in mothers receiving probiotics *vs*

1340 pg/mL in mothers receiving placebo; p = 0.018). The risk of developing atopic eczema during the first 2 years of life in infants whose mothers received probiotics was significantly reduced compared to infants whose mothers received placebo (15% and 47%, respectively; RR 0.32; p = 0.0098). It is likely that consumption of non-commercial food products provides a higher load of micro-organisms compared to consumption of commercial dry foods, which is extruded/baked and therefore more sterile, supporting the "hygiene hypothesis" above. When dry foods are heated, bacteria are killed, and they become more sterile. Also, some of the ingredients given to bitches during lactation are probiotics, such as fermented milk products, and can possibly be considered comparable to those given in the study by Rautava *et al.* [16]. The question is whether the puppies are exposed to the non sterile food particles through the environment by products given to the bitch or whether the puppies are exposed through the milk.

An introduction of diverse solid food during the first four months increased the risk of eczema in childhood 2.5 times in relation to those children not being introduced to solid food during the first four months [17]. In our study there was no significant difference between cases and controls for the time of introducing the first solid food, or when weaning was completed.

Laitinen & Isolauri [18] have shown that dietary lipids, especially long-chain polyunsaturated fatty acids, regulate immune function and may modify the adherence of microbes in the mucosa thereby contributing to host-microbe interactions. The properties of specific dietary compounds in optimal combinations and the joint effects of nutrients can only be exploited in the development of specific prophylactic and therapeutic interventions. In the present study we knew nothing about the exact nutrient status of each dog, or of the fatty acid content and composition. The dietary fatty acid composition has a large impact on the well-being of the skin in individuals with CAD [19]. In future intervention studies, it would be important to make use of specific nutrient profiles that suit any life-stage studied regardless if it is a commercial and processed or a non commercial non processed diet that is given.

As our study had rather few individuals, it would be important to further investigate some of the parameters in detail with a higher number of individuals. Although answers on feeding of the bitch reflect rather historical information from the breeders, we have previously validated collection of such material from a similar population [11]. Given the strength of the association for the interaction it is unlikely to be a spurious finding.

For this case-control study we have chosen cases and controls from three high-risk breeds boxer, English bullterrier and West Highland white terrier in a population of Swedish dogs. It is not known to what extent these results are applicable also to other breed populations. When evaluating the data, we noted that breeders use extremely different feeding regimens regarding how and when they give different foods and ingredients to pregnant and lactating bitches and their puppies. There was not enough power in this study (nor was it designed for this purpose) to determine whether these differences were specific to individual breeders or whether there was some relationship to the breed per se. It would be advisable to examine differences in dietary intake and dietary exposure in a combined study of environmental and genomic factors and in a larger sample also in other breeds with and without increased risk for CAD.

CONCLUSION

Based on the data presented in the study, it would seem prudent to feed bitches some non-commercial animal products, including meat during lactation. The results support the hypothesis that exposure to non sterile food constituents very early in life might protect from CAD. The question remaining is if the puppies are exposed through lactation or by environmental exposure.

ABBREVIATIONS

CAD = Canine atopic dermatitis

LUPA = EU project, named after female-wolf that fed the twin founders of Rome, and backed with EUR 12 million and will end in 2012

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