Comparison of Immediate Skin Test Reactions in Clinically Normal and Self-mutilating *Psittaciformes*

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Abstract

Forty one Psittaciformes with no evidence of self-mutilation were subjected to intradermal skin testing along the apteria between the sternal pterylae using saline, histamine and aqueous allergen extracts of rye grass, wheat, canary, oat, maize, grain mill dust, *D. pteronysinus, D. farinae,* and sunflower. Intradermal skin testing also was applied in fifteen Psittaciformes showing clinical evidence of self-mutilation. Ninety three percent (14/15) of clinically self-mutilating birds in this study showed wheal reactions to one or more allergen compared with only 2% (1/41) of normal birds. This was a highly significant statistical difference and suggested that environmental allergens may be associated with self-mutilation in Psittaciformes. Only 32% of normal birds and 67% of self-mutilating birds tested showed wheal reaction in response to histamine, with seven individuals not reacting to histamine yet still showing intradermal reaction to allergens. The inconsistent response suggests that birds vary in their sensitivity to histamine and/or histamine may not be the only mediator able to induce wheal reactions in Psittaciformes. Four clinically affected birds that reacted to specific allergens showed the same reactions on subsequent retesting. Further investigation is under way to assess whether skin testing coupled with avoidance or hyposensitisation may be a useful procedure for the diagnosis and treatment of some cases of self-mutilation in Psittaciformes.

Introduction

Feather picking is a common clinical presentation in avian practice that can be frustrating in terms diagnosis and treatment. External and internal parasites; bacterial, fungal, viral and other infectious agents; nutritional imbalances, sexual or psychological problems, stress, abdominal discomfort caused by internal organ pathology, heavy metal toxicity, and poor husbandry have all been incriminated as causes.[1-3] In many cases the cause of the disorder is not established.

Pruritus can cause severe self trauma in other animal species such as the cat, dog, horse and human. Food allergies and atopic dermatitis, an inherited IgE mediated hypersensitivity to airborne allergens, can cause dramatic pruritus when sensitised individuals are exposed to offending environmental allergens. An underlying type I hypersensitivity is reported to be responsible for allergen-specific IgE production and subsequent mast cell degranulation triggered by crosslinking of surface-bound IgE antibodies by the offending allergens.[4-6] Immediate skin test reactivity has been used to identify offending allergens in cats, dogs, horses and humans with atopic dermatitis. Subsequent hyposensitisation or allergen avoidance has been a successful treatment modality in these species.

There are parallels between hypersensitivity reactions in birds and mammals. Mast cells have been identified in birds and cell products such as histamine and serotonin are released on degranulation, but a predecessor, IgY, has been implied to play the role of mammalian IgE in avian species.[7,8] Anaphylactic reaction (type 1 hypersensitivity) has been documented in pigeons receiving a paramyxovirus type 1 vaccine, [9] and clinical evidence suggests that type

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1 allergic hypersensitivity reactions to air-borne allergens may also be associated with asthma-like syndromes in South American Psittaciformes.[10] Delayed hypersensitivity reactions have been studied in chickens and are believe to play a role in post vaccination granuloma formation in both psittacines and poultry.[11]

Therapeutically, some Psittaciformes will show decreased self-mutilation in response to the use of glucocorticoids, suggesting an allergic or autoimmune basis to the condition. Unfortunately, apart from side effects recognised in mammalian species, the use of glucocorticoids in birds may induce fault-lines in newly forming feathers. Antihistamines such as diphenhydramine, may also be useful in reducing pruritus in some cases of self-mutilation, again suggesting a possible allergic basis to the problem. Anecdotally, aviculturalists and veterinarians have noted that placing birds on elimination diets will sometimes reduce pruritus, suggesting that food allergies may play a role in self-mutilation.

Because of the variable response to empirical treatment for allergies, it would be useful to be able to establish if specific allergens are associated with self-mutilation in individual birds and to develop treatment plans based on these known or suspected allergens. The use of intradermal skin testing to identify potential allergens in Psittaciformes has not previously been reported. This study evaluated immediate intradermal skin test reactivity to a limited array of environmental allergens in normal Psittaciformes and in birds showing clinical evidence of self-mutilation

Material and Methods

Psittaciformes from a local pet shop were examined for evidence of self mutilation in December 1997 and January 1998. Forty one birds of nine different species, showing no evidence of self-mutilation, were used for this investigation. These included six Peach-faced Lovebirds (*Agapornis roseicollis*), six Galahs (*Eolophus roseicapillus*), five Alexandrine Parrots (*Psittacula eupatria nipalensis*), five Long-billed Corellas (*Cacatua tenuirostris*), three Sulphur-crested Cockatoos (*Cacatua galerita*), six Cockatiels (*Nymphicus hollandicus*), four Rainbow Lorikeets (*Trichoglossus haematodus*), three Eclectus Parrots (*Eclectus elegans*), and three Pale-headed Rosellas (*Platycercus adscitus*). Allergens were selected based on availability and suspected relevance for birds kept indoors (Table 1).

Each bird's chest was swabbed with alcohol to part the feathers and reveal the apteria between the sternal pterylae. Six dots were marked along the keel with an indelible black marking pen. Intradermal injections were placed on either side of the marked dots by gently inserting a 26 gauge intradermal needle, bevel up, at an angle of roughly 10 degrees and injecting 0.02 ml of fluid to produce a flat bleb (Fig. 1).

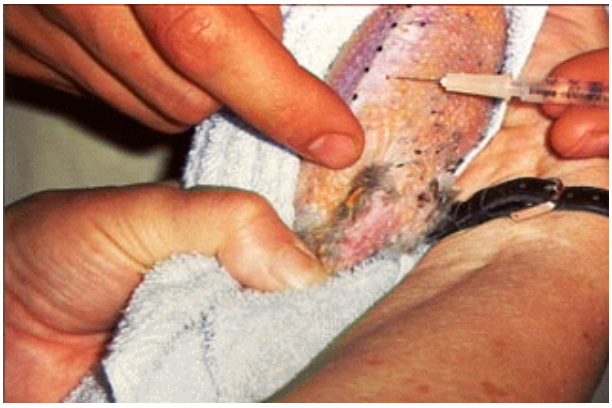

Fig. 1. Rainbow Lorikeet, case # PRA1/98, intradermal skin test. Initial intradermal injections (sites marked with black ink dots) along either side of the keel bone. Distinct blebs are present at injection sites.

Control solutions and allergens included saline, histamine, canary, rye, oat, wheat, maize, grain mill dust, *D. pteronysinus*, *D. farinae* and sunflower. The allergen concentration was typically 4000 protein nitrogen units (PNU)/ml, however dust mites were tested at 120 PNU/ml. Blebs were visually examined at 5 minutes and 15 minutes post injection in normal room light and again with a laterally placed focal light source. For consistency, all injections were made and skin test results assessed by the same person (Mueller), who was experienced in reading skin test results in dogs and cats. Reactions were considered positive if a wheal was produced which exceeded the diameter of the negative control. Hematoma / erythematous reactions without wheal formation were also noted.

Fifteen Psittaciformes showing evidence of self-mutilation presented at one of the author's (Macwhirter's) practice were also subjected to intradermal skin testing using the procedure described above. These included seven Peach-faced Lovebirds, two Galahs, two Sulphur-crested Cockatoos, one Cockatiel, one Rainbow Lorikeet, one Pink Cockatoo (*Cacatua leadbeateri*), and one Little Corella (*Cacatua sanguinea*). Table 2. These self-mutilating birds were negative on loupe and microscopic examination for external parasites, histories did not suggest a sexual or psychological cause for their condition and whole body radiographs were not remarkable. In two cases additional allergens (Alternaria and oak) were used where the bird's history was suggestive that a particular allergen might be significant. Four birds were subject to repeat allergen testing several weeks following their initial test (Fig. 2)

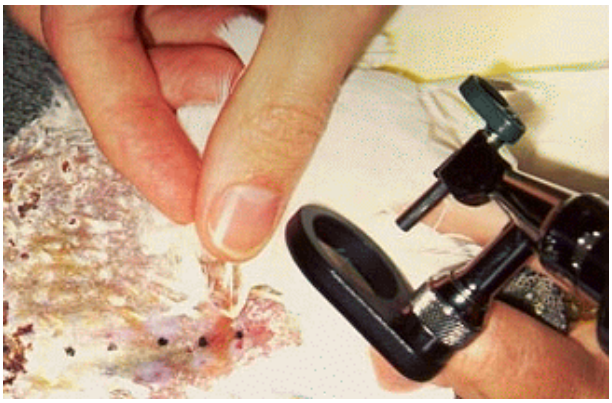

Fig. 2. Sulphur-crested cockatoo, Case # GUCC/98, intradermal skin test. Fifteen minute reaction time showing 2+ reactions (wheals) to *D. pteronysinus, D. farinae,* and sunflower antigens.

Depending on the individual case, owners of birds showing self-mutilation were advised to remove allergens to which the bird had reacted from the bird's environment or diet. Where this was not practical owners were offered hyposensitisation treatment with vaccine prepared from the allergen(s) to which their bird reacted. Other treatment modalities were applied if concurrent disease problems such as heavy metal toxicity or psittacosis were identified. Elizabethan collars were applied as a temporary mechanism to stop self-mutilation while the underlying disease was treated.

Results

Results for normal Psittaciformes are shown in Table 1, those for self-mutilating birds in Table 2. Using a non-paired student T test there was a highly significant statistical difference between the number of self mutilating birds showing wheal reactions to one or more of the allergens tested (14/15) compared with reactions seen in control birds (1/41), (P value of 0.0001).

4 Comparison of Immediate Skin Test Reactions

Table 2

Wheal reaction to skin testing in fifteen clinically self mutilating Psittaciformes

	Reactions (graded from 0 to 4+)											Total allergen reactions
Patients	**Histamine**	**Saline**	**Canary**	**Rye**	**Oat**	**Wheat**	**Maize**	**Grain Mill Dust**	***D. pteronysinus***	***D. farinae***	**Sunflower**	
PF Lovebird (CAL/97)	1+	0	0	0	0	0	1+	0	0	0	ND	1
PF Lovebird (PRA1/97)*	1+	0	0	0	0	0	0	0	0	0	1+	1
PF Lovebird (PRA2/97)*	1+	0	0	0	0	0	0	1+	0	0	0	1
PF Lovebird (NOW1/97)	1+	0	0	0	0	0	1+	0	0	0	0	1
PF Lovebird (NOW2/97)*	1+	0	0	0	0	0	0	0	1+	0	0	1
PF Lovebird (MAL1/97)	1+	0	0	0	0	0	0	0	0	0	0	0
PF Lovebird (MAL2/97)	0	0	0	0	0	0	0	0	0	0	1+	1
Cockatiel (PANT/97)	1+	0	0	0	0	0	0	0	0	1+	0	1
Galah (KLEI/97)	1+	0	0	0	0	0	1+	1+	0	0	0	2
Galah (NIMB/97)*	1+	0	0	0	0	0	0	0	1+	0	0	1
Little Corella (KARA/97)	2+	0	0	0	0	0	0	0	0	0	2+	1
SC Cockatoo (WATT/97)	0	0	0	0	0	0	0	0	0	0	2+	1
SC Cockatoo (GUCC/98)	0	0	2+	0	0	0	0	0	2+	2+	2+	4
MM Cockatoo (MCKE/98)	0	0	0	0	0	0	0	0	0	0	1+	1
Rainbow Lorikeet(PRA1/98)	0	0	0	0	2+	0	0	2+	1+	2+	0	4
Totals												
Wheal formation (+/- erythema)	10	0	1	0	1	0	3	3	4	3	6	14
%	67%	0%	7%	0%	7%	0%	20%	20%	27%	20%	43%	93%

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PF Lovebird (CAL/97)	1+	0	0	0	0	0	1+	0	0	0	ND	1
PF Lovebird (PRA1/97)*	1+	0	0	0	0	0	0	0	0	0	1+	1
PF Lovebird (PRA2/97)*	1+	0	0	0	0	0	0	1+	0	0	0	1
PF Lovebird (NOW1/97)	1+	0	0	0	0	0	1+	0	0	0	0	1
PF Lovebird (NOW2/97)*	1+	0	0	0	0	0	0	0	1+	0	0	1
PF Lovebird (MAL1/97)	1+	0	0	0	0	0	0	0	0	0	0	0
PF Lovebird (MAL2/97)	0	0	0	0	0	0	0	0	0	0	1+	1
Cockatiel (PANT/97)	1+	0	0	0	0	0	0	0	0	1+	0	1
Galah (KLEI/97)	1+	0	0	0	0	0	1+	1+	0	0	0	2
Galah (NIMB/97)*	1+	0	0	0	0	0	0	0	1+	0	0	1
Little Corella (KARA/97)	2+	0	0	0	0	0	0	0	0	0	2+	1
SC Cockatoo (WATT/97)	0	0	0	0	0	0	0	0	0	0	2+	1
SC Cockatoo (GUCC/98)	0	0	2+	0	0	0	0	0	2+	2+	2+	4
MM Cockatoo (MCKE/98)	0	0	0	0	0	0	0	0	0	0	1+	1
Rainbow Lorikeet(PRA1/98)	0	0	0	0	2+	0	0	2+	1+	2+	0	4
Totals												
Wheal formation (+/- erythema)	10	0	1	0	1	0	3	3	4	3	6	14
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Wheal formation, when it occurred, was subtle with the most pronounced reactions no more than 4 mm diameter and elevated 0.5 mm. (2+ reaction). The laterally placed focal light source was useful in assessing reactions. Reactions at 5 minute and 15 minutes were similar although, in some cases, wheals became slightly smaller by 15 minutes. Erythema or hematoma without wheal formation was seen in 15/660 (2%) of the intradermal injections carried out, in two cases even with the saline control. None of the birds showed any adverse reaction to the skin testing.

Response to histamine was inconsistent, both in normal and clinically affected birds. Overall 32% of the normal birds and 67% of self-mutilating birds tested showed wheal formation in response to histamine. While numbers of birds tested were not sufficient to establish statistical significance, species variation in response was seen with none of the Alexandrine Parrots, Long-billed Corellas, Rainbow Lorikeets, or Sulphur-crested Cockatoos (either clinically affected or normal birds) reacting to histamine while 12/13 Peach-faced Lovebirds, 6/8 Galahs, 2/3 Eclectus Parrots, and 2/7 Cockatiels reacted. None of the normal or self-mutilating birds showed wheal reaction to saline, although two normal birds showed slight erythema/hematoma reactions to saline.

Only 1/41 (2%) of the normal birds tested showed immediate skin test reactivity in response to any of the allergens tested. This was a Long-billed Corella reacting to sunflower. 14/15 (93%) of the self mutilating birds showed wheal reaction to one or more of the allergens tested, of these two birds reacted to four allergens, one bird reacted to two allergens and the remainder reacted to only one. The allergens which most frequently induced reactions included sunflower (6/14), the house dust mites *D. pteronysinus* (4/15) and *D. farinae* (3/15), maize (3/15) and grain mill dust (3/15). There was only one reaction each to canary and oat and there were no reactions to wheat or rye. In four cases birds retested after several weeks showed the same test results to the same allergens. (Table 2)

Five clinically affected birds, as well as one normal Long-billed Corella, showed wheal reactions to allergens even though they did not react to histamine. One bird tested against oak based on clinical history did not react. Another tested against *Alternaria* mould did react.

Many of the birds tested have been long term self-mutilators so it will be some time before meaningful assessment of response to treatment can be made. An up date will be presented at the time of the conference.

Discussion

The highly significant difference in the proportion of self-mutilating Psittaciformes (93%) showing at least one wheal reaction in response to intradermal skin testing against nine environmental allergens compared with control birds (2%) could suggest that allergens may play a role in the development of self-mutilation. Alternatively, inflamed skin of self-mutilating birds may be randomly more likely to exhibit irritant reactions upon intradermal injections. However, wheal reactions occurred to a variety of allergens and reactions varied between individual birds. In four patients that were retested, wheal reactions were the same as had been observed initially. These results suggest that response to specific allergens in individual birds induced the wheal reactions rather than the wheals being non-specific. However, additional trials on the replicability of test results in individual birds will be needed to establish this.

Interpreting test results presented a challenge and will require much further study. Overall reactions were subtle and short-lived compared with those seen in canine patients and reminiscent of feline skin testing reactions.[12] None of the wheals seen in the birds tested, either to allergens or histamine, were greater than 4 mm x 0.5 mm. These were graded 2+, compared to with a 4+ grading of the more prominent reactions routinely seen with histamine in canine patients. This may be due to avian IgY being less effective in triggering mast cell degranulation than the evolutionarily more specialised mammalian IgE. Alternatively the birds tested may have been stressed by the procedure and released endogenous glucocorticoids which may have interfered with skin testing in a similar way suspected in cats. The number of dermal mast cells and the amount of mediators released may be much smaller in birds than in mammalian species.

Hematoma / erythema was seen with 2% of the injections given, including saline, histamine and allergens. Although it occurred more frequently with histamine than with saline, it was considered non-specific and perhaps sometimes associated with patient movement during injection or less than ideal injection technique. If hematoma / erythema occurs without clear wheal formation, repeat injection at a different site might help to clarify results.

Reactions to histamine were variable with only 32% the normal birds and 62% of the clinically affected birds showing wheals. Histamine receptors on endothelial cells are present in mammals and histamine induced activation of endothelial cells causes leakage of serum and exocytosis of inflammatory cells contributes to wheal and flare reaction in mammalian species. Some birds may lack histamine receptors on endothelial cells or alternatively, suppression of histamine-induced wheals by endogenously released glucocorticoids may occur. If the wheal reaction is triggered by histamine, as is known to occur in mammals, endogenous cortisone release would not account for the 5/15 (33%) of self-mutilating birds that showed wheal reactions to allergens even though they failed to react to histamine. It is possible that histamine may not be the only mediator of mast cell degranulation in Psittaciformes.

The apteria between the sternal pterylae in the birds tested provided a limited area on which place 11 intradermal injections, especially in small species. Care needed to be taken in placement of the injections to ensure the fluid was placed accurately and intradermally to produce an obvious bleb. Practice and magnification using a loupe may be helpful for inexperienced operators to refine technique. As wheal reactions in some birds began to decrease after 15 minutes, approximately 10 minutes is suggested as the best time to assess reactions but, as the reactions are often subtle, checking at 5 minutes and 15 minutes is useful. The site of skin testing was not visible once the feathers were dry and replaced in their normal positions in normal birds. While the skin testing procedure described could be applied in a general practice setting, allergens need to be prepared fresh, preferably weekly, which would be inconvenient for practices with low avian dermatology case loads.[13]

Food allergies are generally associated with type 3 (immune complex) hypersensitivity in mammals. While there is little correlation between skin testing results and food allergy in dogs, many humans with food allergies will react to food allergens on skin testing.[14] Oat, wheat, rye, canary and maize used for skin testing in this series were pollens. Whether there is allergic cross reaction between pollen and seeds fed in bird diets is not known. Other environmental allergens such as tree, grass and weed pollens, insects, moulds or tobacco may play a role in initiating allergic conditions. One bird, that had a history of possible exposure to mould, tested positive on skin testing for Alternaria. As space available for skin testing in birds is limited, decisions as to relevant allergens for which to test need to be taken carefully. As none of the birds tested reacted to wheat or rye, it I possible that these may be less likely to induce allergic reactions. Based on patient history, other allergens such as millet or safflower might have been relevant and worth testing but these were not available at the time of the study.

Treatment for self-mutilating birds showing positive reactions to skin tests in this series have been instituted using elimination diets, allergen avoidance and vaccines. Updated information on these cases will be available at the time of the conference.

Sources and Manufacturers

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Acknowledgments

Thanks are gratefully extended to Burwood Birds and Pets for their help with in this study.

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