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THE USE OF INTRADERMAL ALLERGY TESTING FOR ALLERGIC DERMATITIS IN PTEROPID BATS AND TREATMENT WITH ALLERGEN SPECIFIC IMMUNOTHERAPY: A CASE SERIES

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Abstract: This case series describes the diagnosis of allergic dermatitis and management with allergen-specific immunotherapy (ASIT) based on intradermal allergy testing (IDAT) and adjunctive medical therapy in six pteropid bats; five large flying foxes (*Pteropus vampyrus*); and one variable flying fox (*Pteropus hypomelanus*). The cases ranged from 2 to 15 yr of age at the time of presentation. Clinical signs varied between individuals and included moist ulcerative cutaneous lesions in nonhaired skin, blepharoconjunctivitis, alopecia, and pruritus. All bats underwent IDAT under general anesthesia, and reactive allergens included a mixture of grasses, trees, weeds, and biting insects. Three of the six cases (50%) had reformulation of the ASIT before control of clinical signs was seen, and two bats were treated with the addition of oclacitinib (Apoquel). Severe adverse effects were not identified; however, one bat had self-limiting swelling at the immunotherapy injection site. All six cases showed improvement of clinical signs and perceived comfort level, including in subsequent allergy seasons.

INTRODUCTION

Allergic dermatitis is traditionally associated with type 1 hypersensitivity resulting from an alteration in epidermal barrier function, involving activation of mast cells by IgE bound to specific allergens.²¹ In veterinary medicine, it is best documented in domestic animals, including dogs, cats, and horses.^{16,21,26} It has also been described in zoologic species, including a Bactrian camel (*Camelus bactrianus*), fossa (*Cryptoprocta ferox*), and black leopard (*Panthera pardus*).^{11,22,25} Clinical signs in affected species include seasonal pruritus and moist dermatitis, commonly affecting axillae, inguinal regions, pinnae, and feet.²¹

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Bats of the genus *Pteropus* are often kept in zoologic and rehabilitation settings. Cutaneous lesions are common; a survey conducted in Europe, North America, and Australasia found a prevalence of skin disease in 38% of captive *Pteropus*.¹⁰ Skin disease, primarily on the wing membranes, can lead to increased electrolyte and protein loss from ulcerative lesions, which can result in significant morbidity.¹⁰ Reported skin diseases in bats include fungal dermatitis, bacterial dermatitis, vitiligo, and allergic dermatitis.^{4,10,14,27}

Intradermal allergy testing (IDAT) is a diagnostic tool performed during the workup of allergic dermatitis and used to document the type 1 hypersensitivity reaction associated with a particular allergen. The intradermal reaction to a dilution of allergen is semiquantitatively assessed compared with a positive (histamine) and negative (saline) control.²¹ Species-specific serum allergen-specific IgE immunoassays offer an alternate means of testing; however, validation has only been performed in a few domestic species.²⁸ The only validated immunoglobulin assay in *Pteropus* spp. tests for IgG after vaccination but not IgE.²⁹

Protocols used for allergen-specific immunotherapy (ASIT) depend on the clinical scenario. It can be administered either as injections of subcutaneous immunotherapy (SCIT) or oral administration of sublingual immunotherapy (SLIT). In most cases, ASIT is considered a lifelong treatment meant to control the degree of clinical signs rather than cure the disease. In some individuals,

reformulation is required as new allergies develop or as allergies progress in severity.³

ASIT is being used with increasing frequency in zoologic medicine.^{11,22} However, clinical efficacy has not been sufficiently studied in nondomestic species, and the use has been documented primarily in single case reports. We report six bats of the genus *Pteropus* diagnosed with allergic dermatitis and treated with ASIT, in addition to symptomatic therapy for control of their clinical signs.

CASE REPORTS

Five large flying foxes (*Pteropus vampyrus*) and one variable flying fox (*Pteropus hypomelanus*) were evaluated by the Zoological Medicine Service at the University of Florida College of Veterinary Medicine for clinical signs suggestive of allergic dermatitis, including ulcerative skin lesions, alopecia, pruritus, and blepharoconjunctivitis (Fig. 1). The bats ranged from 2 to 15 yr of age at the onset of clinical signs and included male ($n = 2$) and female ($n = 4$) bats. Case information and clinical signs are summarized in Table 1.

The bats were managed at a private zoologic institution in north-central Florida. Bats were housed in outdoor, circular enclosures with access to an indoor shelter. Several varieties of plants grew within and around the enclosures. Select plant species, including wax myrtle (*Myrica* sp.) and sweet gum (*Liquidambar styraciflua*), were offered for browse. The primary diet included a mixture of fruits and vegetables and a proprietary vitamin supplement (Lubee Fruit Bat Vitamin and Mineral Supplement, HMS Zoo Diets Inc, Bluffton, IN 46714, USA).

Prior to testing, all bats underwent a 4-wk washout period of topical and systemic anti-inflammatory medications and antihistamines, which may interfere with IDAT. Animals were anesthetized with isoflurane delivered via face-mask. A rectangular region was shaved along the dorsal midline, and injections (0.1 ml) were administered intradermally using a syringe with a 27-gauge needle, approximately 1.5 cm apart (Fig. 2). Allergen extracts (Greer Veterinary Allergy, Lenoir, NC 28645, USA) were administered at standard concentrations used in domestic species. Histamine (0.0275 mg/ml, Greer Veterinary Allergy) was administered as a positive control, and sterile 0.9% saline was administered as a negative control. The allergen test sites were immediately assessed after injection and again 10 to 15 min later. The injection sites were subjectively scored from 0 (no reaction) to 4 (very strong

reaction) based on comparison to the controls by a board-certified dermatologist. A summary of positive allergens in each case are listed in Table 2.

Allergens selected for inclusion were based on clinical history, seasonal variation in clinical signs, commercial availability from the manufacturer, and positive reactions identified through IDAT. Unless otherwise stated, the bats were placed on a subcutaneous ASIT protocol (SCIT) consisting of a three-vial schedule, with each vial containing gradually increasing concentrations of allergens to reach a maintenance vial (vial 3). The concentration of the third vial was 20,000 protein nitrogenous units (PNUs) of total allergen per milliliter. Vial 1 had 1% of the concentration of the maintenance vial, whereas the second vial contained 10%. The administration of the vials was in two phases: an initial loading phase followed by a maintenance phase. The loading phase occurred over the first 12 wk. The first vial had a starting volume of 0.1 ml administered every 2 d and gradually increasing by 0.1-ml increments to reach 1.0 ml total volume after 2 wk. The second vial had a starting volume of 0.1 ml administered every 3 d and gradually increasing volume by 0.1-ml increments to reach 1.0 ml after 2 wk. The third vial had a starting volume of 0.1 ml, increasing to 1.0 ml injected every 3 d for 2 wk, every 5 d for 2 wk, and then every 10 d for 2 wk. The maintenance phase followed with a dose of 1.0 ml from vial 3 administered every 3 wk. The bats were briefly manually restrained for SC injection in the interscapular region. The bats also received symptomatic treatment with antihistamines, along with anti-inflammatories, antimicrobials, and omega-3 fatty acids, as necessary.

Case 1

A 15-yr-old female *P. vampyrus* presented in April 2014 for evaluation of a cluster of four, 3- to 5-mm-diameter, moist ulcerative cutaneous lesions over the left carpus (Fig. 1A) and multifocal firm, nodular lesions in the right patagium (suspected mineralization) comprising approximately 20% of the patagial surface. The patient was frequently observed grooming these areas. The lesions expanded in size and coalesced into three circular lesions, covering most of the carpus, despite treatment with loratadine (Claritin, Bayer Inc, Boca Raton, FL 33481, USA; 1.0 mg/kg PO, q24h) and topical ointment: a combination of 1% orbifloxacin, 0.1% mometasone furoate, 1% posaconazole (Posatex, Merck Animal Health, Madison, NJ 07940, USA; topically, q24h for 30 d).



Figure 1. (A) Small circular to ellipsoid ulcerative cutaneous lesions with erythema and scar tissue formation on the left carpus of an adult female large flying fox (*P. vampyrus*) (case 1). (B) Severe moist ulcerative cutaneous lesions on the propatagium of an adult female large flying fox (*P. vampyrus*) (case 1). (C) Moderate ulcerative cutaneous lesion on the propatagium of an adult female large flying fox (*P. vampyrus*) (case 2). (D) Moist ulcerative lesion along the distal right pinna of an adult male large flying fox (*P. vampyrus*) (case 3). (E) Severe chemosis, conjunctival hyperemia, and mild blepharospasm in the left eye of an adult male large flying fox (*P. vampyrus*) (case 3). (F) Moist ulcerative cutaneous lesions along the left antebrachium and plagiopatagium in an adult female large flying fox (*P. vampyrus*) (case 6).

Table 1. Summary of clinical signs, dates of IDAT, and treatment plan with ASIT in six pteropid bats with allergic dermatitis.

Case	Species	Age at onset (yr)	Onset of signs	Clinical signs	IDAT and ASIT start date	Clinical improvement noted	ASIT reformulation dates
1	<i>Pteropus vampyrus</i>	15	Apr 2014	Ulcerative skin lesions	Jul 2014	Jan 2015	Nov 2015, Aug 2018
2	<i>Pteropus vampyrus</i>	5	May 2003	Ulcerative skin lesions, blepharo-conjunctivitis, alopecia	Jul 2014	Jan 2015	Dec 2016, Aug 2018
3	<i>Pteropus vampyrus</i>	9	May 2010	Ulcerative skin lesions, blepharo-conjunctivitis, alopecia	Jun 2016	Jul 2016	None
4	<i>Pteropus hypomelanus</i>	2	Jul 2017	Alopecia, pruritus	Nov 2017	May 2018	None
5	<i>Pteropus vampyrus</i>	11	Jan 2017	Ulcerative skin lesions, pruritus	Sept 2017	Nov 2017	None
6	<i>Pteropus vampyrus</i>	9	Sept 2008	Ulcerative skin lesions, blepharo-conjunctivitis, alopecia	Aug 2013	May 2014	Sept 2015, Jan 2018

**Figure 2.** Anesthetized large flying fox (*P. vampyrus*) undergoing IDAT. The dorsum from the cranial ridge of the scapulae to the pelvis was clipped and a silver marking pen was used to orient the injections of allergen extracts.

Histopathology showed a mild perivascular and interstitial lymphoplasmacytic and histiocytic dermatitis, moderate acanthosis, spongiosis, and orthokeratotic hyperkeratosis. There were also multifocal and focally extensive accumulations of mineral within varying levels of the dermis associated with granulomatous and mixed inflammation, fibrosis, and granulation tissue. In July 2014 (91 d after presentation), IDAT was performed with positive reactivity to 10 plant species, including grasses, trees, and weeds (Table 2). ASIT was initiated, and by January 2015 (282 d after presentation), the lesions were healed, with a small amount of scar tissue remaining. Systemic antihistamines were discontinued in October 2015. There was a decrease in visible and palpable wing mineralization and subjective reduction in observed grooming behaviors.

Despite ongoing ASIT treatment, the lesions recrudesced in November 2015 (560 d after presentation) and August 2018 (1,570 d after presentation); however, the lesions were subjectively smaller than at initial presentation. Follow-up IDAT was performed at both time points. Additional positive reactions were noted to three tree species, *Malassezia* sp., biting midges (*Culicoides* sp.), and deerfly (*Chrysops* sp.) (Table 2). The immunotherapy was reformulated at each time point but did not include insect allergens because of lack of product availability and institutional protocol. Two weeks after the first reformulation, during the repeat initial loading phase of ASIT, the patient had mild focal erythema and swelling at the immunotherapy injection site in the interscapular region, which

Table 2. Summary of reactive allergens from IDAT in six pteropid bats with allergic dermatitis.

Allergen	Classification	Case 1			Case 2			Case 3			Case 4			Case 5			Case 6		
		Jul 2014	Nov 2015	Aug 2018	Jul 2014	Dec 2016	Aug 2018	Jun 2016	Nov 2017	Sept 2017	Aug 2013	Sept 2015	Mar 2018	Sept 2017	Aug 2013	Sept 2015	Mar 2018	Sept 2017	Aug 2013
<i>Alternaria</i> sp.	Ascomycete fungi													2		2			
<i>Malassezia</i> sp.	Yeast fungi		2												2	2			
<i>Culicoides</i> sp.	Biting insect		2		3	3								4	3		3		
Deer Fly (<i>Chrysops</i> sp.)	Biting insect			3				4							4				
Bahia Grass (<i>Paspalum notatum</i>)	Grass	3		3	2		2								3				
Kochia (<i>Bassia scoparia</i>)	Grass	3													2				
American Elm (<i>Ulmus americana</i>)	Tree														3				
Bald Cypress (<i>Taxodium distichum</i>)	Tree	3			3		2			1									
Hickory (<i>Carya tomentosa</i>)	Tree				3										1				
Pecan (<i>Carya illinoensis</i>)	Tree	3			3										3				
Red Mulberry (<i>Morus rubra</i>)	Tree	3													3		3		
Willow (<i>Salix</i> sp.)	Tree	3	2			2			3	2				3	3		3		
Red Cedar (<i>Juniperus virginiana</i>)	Tree		2	2				4		3				3	2		3		
Live Oak (<i>Quercus virginiana</i>)	Tree		2	2			2			4				4	2		3		
Pine Tree (<i>Pinus</i> sp.)	Tree		2	3	3		3	4		2				2	4	4	2		
Wax Myrtle (<i>Myrica</i> sp.)	Tree	2			2										2				
<i>Melaleuca</i> sp.	Tree		2			2	2		4	2				2	2				
Orange Tree (<i>Citrus</i> sp.)	Tree					2		3	3	3				3	2	2	3		
Palm Tree (<i>Arecaceae</i> sp.)	Tree	2		3		2	2	4	2										
Sweet Gum (<i>Liquidambar styraciflua</i>)	Tree			2		3	2	3	2						3				
Cocklebur (<i>Xanthium</i> sp.)	Weed	3	2	3	2		2	1	3	2				2	2	2	3		
Dog Fennel (<i>Eupatorium capillifolium</i>)	Weed	3		4	2		3												
Goldenrod (<i>Solidago</i> sp.)	Weed	3		4	2		2		2						4				
Ragweed (<i>Ambrosia</i> sp.)	Weed				2		4									4		2	

Each allergen is scored zero to four, with zero indicating no reaction and four being the most reactive.

resolved over 3 d without intervention. The injection was subsequently administered in an alternate location over the shoulder, with no further reactions seen.

The patient had an additional flare-up in April 2019 (1,826 d after presentation) with focal ulcerative lesions on the left carpus and dorsal propatagia (Fig. 1B), despite continuous treatment with the reformulated ASIT from 2018. In June 2019 (2,093 d after presentation) ulcerative lesions were noted on both carpi. The patient was started on oclacitinib (Apoquel, Zoetis Inc, Kalamazoo, MI 49001, USA; 0.7 mg/kg PO, q12h) in addition to the reformulated immunotherapy protocol from 2018. Lesions were healed aside from cutaneous scarring on the left carpus in October 2019 (2,009 d after presentation) and has been controlled through the time of manuscript submission.

Case 2

A 5-yr-old female *P. vampyrus* presented in May 2003 for evaluation of moist ulcerative cutaneous lesions on the dorsal aspect of the carpi. The lesions waxed and waned over 11 yr, with recrudescence primarily in the late spring annually. Treatment with a variety of topical and systemic steroids, antibiotics, nonsteroidal anti-inflammatories, and antihistamines were minimally successful. The patient was most consistently on loratadine (Claritin, Bayer Inc; 1.0 mg/kg PO, q24h) for 3 yr between 2011 and 2014.

In April 2014 (3,988 d after presentation), the ulcerative lesions on the carpi expanded in size, as well as development of bilateral blepharoconjunctivitis, multifocal ulcerative lesions along the digits, and a 1-cm circular lesion of the left propatagia (Fig. 1C). IDAT was performed in July 2014, showing positive reactivity to 10 allergens, including trees, grasses, weeds, and biting insects (Table 2), and subcutaneous ASIT (SCIT) was initiated. Full skin thickness biopsies of the patagium showed a mild to moderate perivascular and interstitial lymphoplasmacytic, histiocytic, and neutrophilic dermatitis, moderate to severe acanthosis, spongiosis, orthokeratotic and parakeratotic hyperkeratosis, and focal crusting. There were also multifocal and focally extensive transdermal irregular foci of mineralization associated with granulomatous and mixed inflammation, fibrosis, and granulation tissue. Complete blood count and serum chemistry was unremarkable.¹⁵ In January 2015 (4,263 d after presentation), the lesions were healed with cuta-

neous scarring, and ASIT was continued at the same frequency for maintenance.

In June 2016 (4,780 d after presentation), moist ulcerative cutaneous lesions were noted on the carpi and digits, as well as multifocal moist alopecia. In December 2016 (4,963 d after presentation), repeat IDAT showed reactivity to five additional plant allergens (Table 2). A new ASIT formulation was created, and a sublingual protocol (SLIT) was initiated once daily, concurrently with the existing subcutaneous protocol (SCIT), based on the IDAT performed in both 2014 and 2016. The lesions were smaller in size on recheck examination 2 mo after starting the concurrent ASIT protocol (4,999 d after presentation).

In July 2017 (5,175 d after presentation), the carpal ulcerations recrudesced and consisted of multifocal to coalescing moist ulcerative lesions ranging from 2 to 8 mm in diameter. The frequency of sublingual therapy was increased from once a day to twice a day, with minimal subsequent improvement. In October 2017 (5,267 d after presentation), skin cytology showed a large number of mixed bacteria, extracellular budding *Malassezia*-like yeasts, and moderate neutrophilic inflammation. Itraconazole (Elanco USA Inc, Greenfield, IN 46140, USA; 15 mg/kg PO, q12h for 6 wk) was prescribed, and skin cytology in February 2018 showed resolution of the fungal organisms. Oclacitinib (Apoquel, Zoetis Inc; 0.7 mg/kg PO, q12h) was prescribed at that time. By March 2018 (5,422 d after presentation), the lesions on the carpi had improved, and only mild erythema remained. Follow-up IDAT was performed in August 2018 (5,587 d after presentation), and reactivity was found to two additional deciduous trees that were not reactors previously, for a total of 11 allergens (Table 2). The SCIT allergen ingredients were reformulated with no changes to the sublingual formulation, which was continued twice daily. By October 2018 (5,632 d after presentation), the carpal lesions were healed with minimal cutaneous scar tissue remaining.

Case 3

A 9-yr-old male *P. vampyrus* presented in May 2010 for evaluation of bilateral blepharoconjunctivitis, which was minimally responsive to diphenhydramine (Benadryl, Johnson & Johnson Inc, Fort Washington, PA 19034, USA; 2 mg/kg PO, q12h for 2 wk). The clinical signs resolved spontaneously after 30 d. In September 2014 (1,584 d after presentation), moist ulcerative lesions were observed along the distal right pinna (Fig. 1D) and both patagia, as well as a small,

firm, nodular lesion on the right dactylopatagium, and severe blepharoconjunctivitis, consisting of chemosis with conjunctival hyperemia and blepharospasm (Fig. 1E). Histopathology of the patagium showed multifocal dermal mineralization associated with granulation tissue, fibrosis, and a perivascular and interstitial lymphoplasmacytic and histiocytic dermatitis. Treatment was not pursued at this time as the lesions waxed and waned over 2 yr.

In May 2016 (2,192 d after presentation), a new moist ulcerative cutaneous lesion was noted on the right first digit, as well as recurrence of the blepharoconjunctivitis. IDAT was performed, which showed reactivity to eight allergens, including biting insects, trees, and weeds (Table 2), and an accelerated SCIT protocol was initiated because of the subjectively fast progression of clinical signs. This consisted of a maintenance injection given every 14 d, instead of every 21 d. Lesions were considered healed in July 2017 (2,618 d after presentation). The SCIT protocol was continued at the 14-d dosing until the time of manuscript submission.

In January 2020 (3,532 d after presentation), the patient was moved to an enclosure that contained palm species, which this patient had reacted to on IDAT performed in 2016, and blepharoconjunctivitis reoccurred despite still receiving SCIT. The patient was moved to a different enclosure that did not contain palm species, and the ocular lesions resolved after 2 d.

Case 4

A 2-yr-old male *P. hypomelanus* presented in July 2017 for generalized pruritus and a 2-cm-diameter circular region of alopecia along the ventral abdomen. Initial diagnostics included a dermatophyte culture and superficial skin scrape, which were both negative. Skin cytology showed moderate extracellular budding *Malassezia*-like yeasts. Histopathology showed a mild perivascular, interstitial, and periadnexal lymphoplasmacytic and histiocytic dermatitis with acanthosis, spongiosis, and scattered “twanged” hair shafts (stretched from licking and pulling), evident of self-trauma.

In November 2017 (127 d after presentation), the area of alopecia expanded to 5 cm in diameter, and the patient continued to be pruritic. IDAT was performed, showing reactivity to biting insects, trees, and weeds (Table 2). The patient was started on SCIT and moved to an enclosure without palm species. Cetirizine (Zyrtec, Johnson & Johnson Inc; 2 mg/kg PO, q24h for 8 wk) was

also prescribed. In May 2018 (311 d after presentation), the degree of pruritus was markedly improved, and cetirizine was discontinued. By June 2018 (340 d after presentation), the pruritus and alopecia had resolved with no recrudescence.

Case 5

An 11-yr-old female *P. vampyrus* presented in January 2017 for evaluation of chronic patagial depigmentation, moist ulcerative cutaneous lesions on the left uropatagium and right digit 1, and pruritus. Topical ointment with antifungal, antibiotic, and steroid (2.3% miconazole nitrate, 0.05% polymyxin B sulfate, 0.5% prednisolone acetate, Surolan, Elanco Animal Health, Indianapolis, IN 51241, USA; 1 drop topically, q12h for 6 wk) was prescribed with limited improvement. IDAT was performed in September 2017 (212 d after presentation), showing reactivity to *Alternaria* sp., biting insects, trees, and weeds (Table 2). Skin cytology showed mild extracellular budding *Malassezia*-like yeasts and cocci. SCIT was initiated using a modified protocol, reaching a total maintenance volume of 0.1 ml over a similar timeline. The lower volume was chosen to help with patient compliance. One month later (250 d after presentation), the lesions were healed, aside from the patagial depigmentation.

In October 2019 (1,003 d after presentation), lesions reoccurred to a lesser degree than initial presentation. Topical miconazole/polymyxin B/prednisolone (Surolan, Elanco Animal Health; 1 drop, topically, q12h for 8 wk) and loratadine (Claritin, Bayer Inc; 1.0 mg/kg PO, q24h for 3 mo) was initiated, and the ulcerative lesions were healed 8 wk later (1,062 d after presentation). No lesions were noted on annual examination in April 2020 (1,186 d after presentation) with no further recrudescence. The bat was still on the SCIT protocol and symptom-free at the time of manuscript submission.

Case 6

A 9-yr-old female *P. vampyrus* presented in January 2008 for evaluation of moist ulcerative cutaneous lesions on both plagiopatagia. Diphenhydramine (Benadryl, Johnson & Johnson Inc; 2 mg/kg PO, q12h) and amoxicillin-clavulanic acid (Clavamox, Zoetis Inc; 12.5 mg/kg PO, q12h) were prescribed for 2 wk, with the lesions healed at conclusion of treatment.

In August 2013 (2,035 d after presentation), IDAT was performed because of chronic intermittent ulcerative lesions along the wings (Fig.

2F), blepharoconjunctivitis, and cranial alopecia. Results showed reactivity to 16 allergens, including *Malassezia* sp., biting insects, grasses, trees, and weeds (Table 2). Skin cytology showed occasional, extracellular budding *Malassezia*-like yeasts, which resolved with itraconazole (Itrafungol, Elanco USA Inc; 15 mg/kg PO, q12h for 6 wk). SCIT was initiated in October 2013 (2,094 d after presentation). In May 2014 (2,333 d after presentation), the lesions were healed with only minimal cutaneous scarring remaining.

In September 2015 (2,820 d after presentation), the ulcerative cutaneous lesions recrudesced. Histopathology of the patagium showed a moderate perivascular and interstitial lymphoplasmacytic, histiocytic, neutrophilic, and eosinophilic perivascular and interstitial dermatitis with spongiosis, moderate to severe acanthosis, and dermal fibrosis with mild dermal mineralization. Follow-up IDAT showed additional positive reactivity to *Alternaria* sp. and two tree species. The immunotherapy was continued at the initial formulation and not reformulated at that time because of a subjectively small number of additional allergens and need for repeat loading schedule. In January 2016 (2,944 d after presentation), no lesions were present on annual examination.

In January 2018 (3,670 d after presentation), alopecia recurred on the head and shoulders, which became larger over the course of a month. In March 2018, repeat IDAT was performed. Additional positive reactivity was noted to *Culicoides* sp. and two additional plant species: red cedar (*Juniperus virginiana*) and ragweed (*Ambrosia* sp.). Dermatophyte culture was negative. The immunotherapy was reformulated to include newly positive allergens, and by July 2018 (3,880 d after presentation), the ulceration had healed with only cutaneous scarring, the alopecia was resolved, and there was no further recurrence at the time of manuscript submission.

DISCUSSION

Clinical signs of the bats in this series were consistent with allergic dermatitis in domestic species and included moist ulcerative dermatitis, alopecia, pruritus, and blepharoconjunctivitis, consisting of chemosis, conjunctival hyperemia, and blepharospasm. Ulcerative cutaneous lesions were the most immediately identifiable, consistent, and severe of the clinical signs observed. A previous case report of a captive large flying fox (*Pteropus vampyrus*) in northern California with allergic dermatitis displayed moist dermatitis, alopecia, and conjunctivitis, similar to the bats

identified in this series.¹⁴ That patient, however, did not have focal ulcerations as identified in our cohort, which may be because of environmental variations in allergen load and individual variation.

Diagnosis of allergic dermatitis can be challenging, because it is considered a diagnosis of exclusion.^{16,21} IDAT was useful in this cohort of bats for providing evidence of a type 1 hypersensitivity to a specific allergen, supporting the diagnosis of allergic dermatitis. It is important to note that a positive test alone does not mean a patient is allergic; IDAT is not a confirmatory test. Importantly, the strength of IDAT score may not correlate with true clinical reactivity. Additional considerations in the differential diagnosis for moist dermatitis and pruritus in bats include ectoparasitism, contact dermatitis, infectious skin disease, and hormonal disorders such as hypothyroidism and hyperadrenocorticism.²¹ The bats in this study are housed in outdoor mesh enclosures with possible exposure to insects. Some cases displayed positive reactions to insect antigens on IDAT. No ectoparasites were noted on physical examination or superficial skin scrape. Dermatophytosis caused by *Trichophyton redellii* has been previously reported in microchiropteran bats, with visible fungal mats growing on the skin resembling white nose syndrome, *Pseudogymnoascus destructans*.²⁰ To the authors' knowledge, dermatophytes have not been reported in association with pathology in megachiropteran bats. Despite this, dermatophyte cultures were performed in cases 4 and 6 and were negative. The bats did not have histologic findings consistent with hormonal etiology or dermatophytosis. Adrenocorticotrophic hormone (ACTH) stimulation testing was performed in cases 1, 2, and 6, as well as thyroid evaluation, including total triiodothyronine (tT3), thyroxine (tT4), and thyroid-stimulating hormone (TSH), in case 6. Interpretation is limited because of lack of validated assays, but there were no overt abnormalities warranting treatment.

The presence of intestinal helminths is potentially associated with the protection of their hosts against allergic sensitization.^{2,9} This bat population has historically been treated for helminths and is largely helminth free; fecal examinations of bats have not identified any helminths in this collection in more than a decade. We were unable to find reports of allergic dermatitis in wild pteropid bats. When treating gastrointestinal helminths, the relative risk of the helminth and

allergic disease should be taken into consideration.

Seasonal variation of clinical signs is a common finding of allergic dermatitis and supported the diagnosis in this cohort.¹⁶ Lesions were first noted in four of the six bats in the late spring, whereas in the other two cases, initial lesions were not noted until fall. The seasonal onset of clinical signs is likely reflective of pollenating seasons of plant species or the prevalence of insect species triggering the hypersensitization response. On the panel of plant species that were tested with IDAT, a total of 23 different plant species were identified as positive reactors in at least one bat. Individual bats developed positive IDAT reactions to varying numbers (between 5 and 16) of these plants (Table 2). At least four of the six bats showed positive reactions to the following plant allergens: wax myrtle (*Myrica* sp.), southern live oak (*Quercus virginiana*), *Melaleuca* sp., palm (*Arecaceae* sp.), red mulberry (*Morus rubra*), and eastern red cedar (*Juniperus virginiana*). These plants all grow in the area surrounding the habitats of these bats but do not grow within the actual enclosures. Only *Melaleuca* sp. and palm (*Arecaceae* sp.) grow naturally within the native ecosystem of the bat species included in this series.

In this cohort, immunotherapy was administered in most cases through an injectable protocol (SCIT). SCIT was chosen because of the less frequent need of administration with this approach as it is administered once every 3 wk compared with twice a day for sublingual administration (SLIT). Both routes of administration are considered equally efficacious in dogs and humans.^{6,19,23} SC injections were comparable in efficacy to sublingual administration for control of clinical disease in humans with birch pollen allergies.¹⁷ In dogs, the use of SLIT was considered effective for the treatment of dust mite sensitivity.⁶ Case 2 did not respond to the SCIT as prescribed, and concurrent SLIT was administered. The efficacy of these two routes of administration is unknown for the treatment of allergic dermatitis in bats.

It is important to note that full long-term resolution was not seen in any bat, but improvement in the overall degree of dermatitis, blepharoconjunctivitis, and pruritus was seen after administration. The immunotherapy protocol was also administered concurrently with symptomatic treatment (systemic antihistamines, topical steroids, etc) for an individualized treatment plan. Significant improvement was not seen with initial symptomatic therapies alone, potentially

because of bats being fastidious groomers and likely removing topical therapies. Lesions started to improve 2 to 6 mo after the addition of immunotherapy. As allergic dermatitis is a life-long immunologic disorder, treatment is provided for long-term reduction in clinical signs and management of acute seasonal flare-ups.²¹ Often, administration of topical ointments, especially those containing steroids, resulted in improvement for short term control of clinical signs, with systemic antihistamines given more consistently and for a more prolonged duration. The use of systemic antihistamines for allergic dermatitis is controversial, without proven efficacy.^{18,30} Often, combination therapy is used for ultimate control, such as the cases in this series.

The treatments were reformulated in these cases because of severity of the clinical signs, lack of improvement, and concern from animal care staff. Despite reformulation of the SCIT, as well as concurrent SLIT, two cases continued to be poorly controlled. Oclacitinib (Apoquel) was prescribed concurrently with immunotherapy in both cases. Oclacitinib is a janus kinase (JAK) inhibitor for the control of pruritus in canine allergic dermatitis.¹³ The dose prescribed in this study was 0.7 mg/kg, which is higher than the canine dosage range, to accommodate the smallest tablet size available. In zoologic medicine, oclacitinib has been used in Andean bears (*Tremarctos ornatus*) with alopecic syndrome.⁸ Controlled studies in zoological species are necessary to determine efficacy of oclacitinib.

No severe side effects were noted with the use of ASIT in this case series. One bat had self-limiting mild swelling at the site of a single injection after a reformulation. Adverse reactions to ASIT in dogs are considered rare and have been reported to include pruritus, urticaria, and hyperactivity. Anaphylaxis is an extremely rare but reported complication.²⁴ A larger sample size is needed to determine the prevalence of adverse effects in bats.

Three of the six bats (cases 1, 2, and 3) had evidence of mineralization within the dermis in the areas of ulceration. Dermal mineralization can form secondary to repeated cutaneous inflammation, systemic corticosteroid use, and hyperadrenocorticism.⁷ Although topical corticosteroids were prescribed in case 1 and may have contributed to the mineralization appreciated within the dermis, cases 2 and 3 did not have topical steroids prescribed before biopsy of the lesions. It is likely that the mineralization in these cases occurred secondary to chronic local inflam-

matory stimulation within the dermis, such as seen with dystrophic calcification.

Malassezia-like yeasts were noted on skin cytology in the majority (four of six) of bats in this series. *Malassezia* is a genus of lipophilic yeasts that can be a part of normal flora in dogs and possibly bats.^{5,12} They are considered a secondary infection and likely to recur if the primary disease is not controlled. In an uncontrolled case series of dogs with *Malassezia* hypersensitivity, SCIT temporally correlated with clinical response, which was defined as reduction in pruritus scores by >50%, in 56% of cases.¹ In our case series, only case 6 was considered hypersensitive to *Malassezia pachydermatitis* based on IDAT. *Malassezia* species in *Pteropus* have not been characterized. This bat had a good clinical response to systemic antifungal treatment with itraconazole for 6 wk, along with the inclusion of *Malassezia* in the ASIT formulation. In dogs with *Malassezia*-associated dermatitis, systemic antifungals may need to be lifelong.¹ The systemic antifungals in this case were discontinued after 6 wk, with no reoccurrence of yeasts identified on cytology.

Allergic dermatitis should be included as a differential diagnosis for any bat with ulcerative cutaneous lesions, blepharconjunctivitis, pruritus, or alopecia. The use of intradermal allergy testing and allergen specific immunotherapy should be considered for the management of allergic dermatitis in megachiropterans.

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