

## CASE REPORT OPEN ACCESS

Dogs

# Successful Management of Refractory Otitis Media Using Allergen-Specific Immunotherapy in a Dog

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## ABSTRACT

**Background:** Allergen-specific immunotherapy (ASIT) is a highly effective treatment for atopic dermatitis. In humans, it has been reported to be significantly more effective than medication alone for the treatment of otitis media. ASIT can also be used in dogs, but it is not typically the first-line treatment for otitis externa and media.

**Objectives:** This case report describes the successful management of refractory otitis media in a dog with frequent abscess recurrence following total ear canal ablation (TECA) using ASIT.

**Methods:** A 9-year-old spayed female American Cocker Spaniel presented with a head tilt and a recurrent abscess adjacent to the left TECA site. A dermatological examination revealed secondary pyoderma. In open-mouth view radiography and CT, fluid in the tympanic bullae and lysis of the tympanic bullae wall were observed. The TECA was repeated twice and anti-inflammatory medication was administered, but the lesions reappeared. As a fundamental treatment, ASIT was included in the therapy.

**Results:** After ASIT, the symptoms did not reoccur, even though the use of prednisolone was gradually reduced and discontinued over a period of two months. Currently, only ASIT has demonstrated progress in managing the patient's condition, even a year after discontinuing other medications. The patient's symptoms have not recurred and are well managed.

**Conclusions:** A case of refractory otitis media, induced by atopic dermatitis, was effectively managed with ASIT over a prolonged period in a dog.

## 1 | Introduction

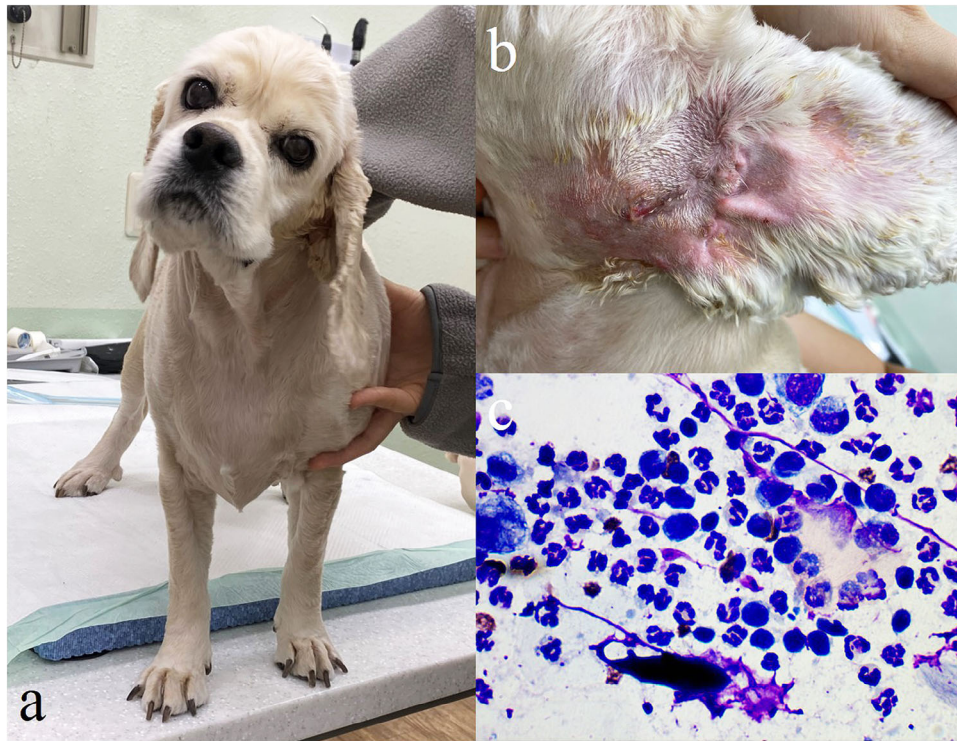
Otitis media is an inflammatory disease that affects the middle ear cavity and occurs secondary in 50% to 80% of cases of chronic otitis externa (Cole et al. 1998; Little et al. 1991). Chronic or recurrent bacterial external ear infections are common in dogs with otitis media (Gotthelf 2004). Clinical signs of otitis media include pain and swelling of the ear canal or pinnae, head tilt, Horner's Syndrome, a drooped lip or ear and loss of the

ability to close the eyelid (Gotthelf 2004; Kern and Erb 1987). Otitis externa has various contributing factors such as primary, secondary, predisposing and perpetuating factors (Bajwa 2019). Among the primary factors, hypersensitivity diseases, including canine atopic dermatitis (CAD) and food allergy, are the most common causes of otitis externa (Saridomichelakis et al. 2007).

CAD is a hereditary, typically pruritic and predominantly T-cell-driven inflammatory skin disease involving interplay

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**FIGURE 1** | Photographs of the dog. (a) Head tilt and (b) abscess adjacent to the left total ear canal ablation (TECA) site were presented on the first visit. (c) Cytology of the lesion showed numerous neutrophils, macrophages, a cluster of *Malassezia* and fagocytosis of bacteria.

between skin barrier abnormalities, allergen sensitization and microbial dysbiosis (Eisenschenk et al. 2024). Allergen-specific immunotherapy (ASIT), administering an increasing amount of specific allergens that cause type 1 hypersensitivity, is considered to be one of the treatment options for recurrent chronic CAD in dogs (Grammar and Greenberger 2018; Olivry et al. 2010). ASIT is an effective treatment for allergic rhinitis/conjunctivitis, allergic asthma, atopic dermatitis and venom hypersensitivity in humans (Moote and Kim 2011). Recently, ASIT has been reported as an effective treatment of otitis media in humans, with significantly higher efficacy than medications alone (La Mantia et al. 2021). ASIT is also used in dogs, but it is not the first treatment option for otitis externa and media (Miller et al. 2013).

This case showed successful management of refractory otitis media using ASIT in a dog with frequent recurrence of abscessation at a total ear canal ablation (TECA) site.

## 2 | Case Report

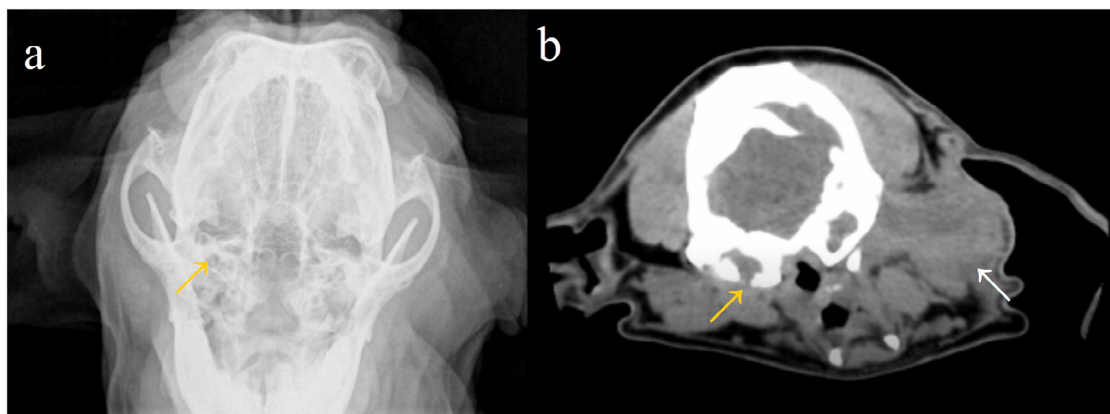
A 9-year-old spayed female American Cocker Spaniel dog presented with a head tilt and recurrent abscess adjacent to a left TECA site (Figure 1a,b). Based on the patient's history, the skin lesions first appeared at the age of 3 years and the patient usually spends their time indoors. TECA surgery was performed bilaterally, but after that, there was continuous exudate in the left TECA site. Therefore, re-operation of left bulla osteotomy was performed twice, but there was no improvement. Glucocorticoids were administered to the patient, which temporarily reduced pruritus and exudate, but the lesion recurred when the drug was withdrawn. Based on Favrot's criteria (Olivry et al. 2010), the

patient was considered to suffer from CAD as 6 of the 8 criteria were fulfilled.

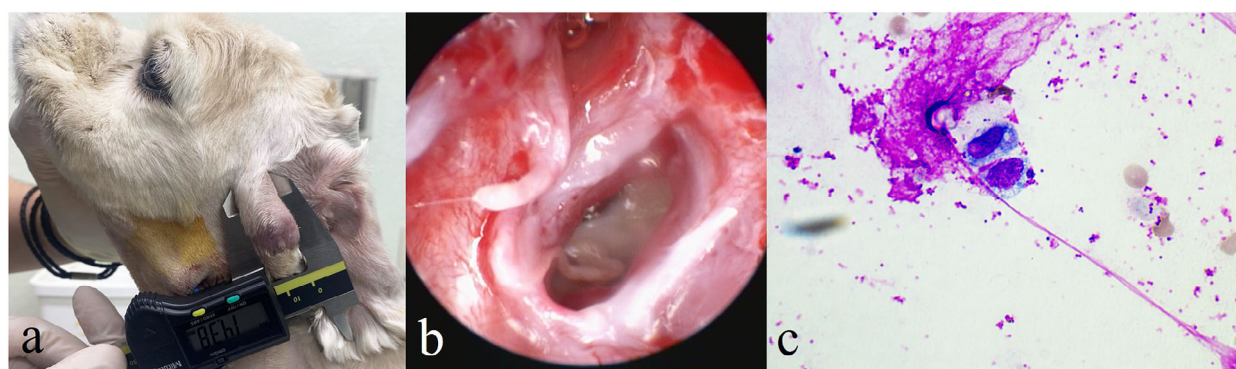
CBC, chemistry and coagulation tests were performed and there were not any remarkable findings except for a thrombocytosis (510 K/ $\mu$ L; reference range 148–484 K/ $\mu$ L). On dermatologic examination, pruritus severity was estimated according to the visual analogue scale (VAS) and lesion severity was estimated using Canine Atopic Dermatitis Extent and Severity Inday (CADESI)-4. The VAS score was 3 out of 10 and CADESI-4 was 22 of 180, which revealed moderate pruritus and mild lesions. On the cytologic evaluation of an impression on the TECA lesions, there were numerous neutrophils, macrophages, a cluster of *Malassezia* and fagocytosis of bacteria (Figure 1c), identifying secondary pyoderma. In open-mouth view radiography and computed tomography (CT), fluid in the tympanic bullae and lysis of the tympanic bullae wall were observed on both sides (Figure 2a,b).

Based on history, dermatologic examination and radiologic findings, the patient was diagnosed with otitis media caused by CAD. Treatment included an immunosuppressive (cyclosporine, 5 mg/kg PO BID; Cipol-N oral solution, CKD Pharm, Seoul, South Korea), antibiotic (cefixime, 10 mg/kg PO BID; Cefixime cap, Withus Pharm, Seoul, South Korea) and antifungal (itraconazole, 5 mg/kg PO BID; Sponazol tab, Nelson Pharm, Seoul, South Korea) agents. The patient's diet was restricted to hypoallergenic dog food and reduced exposure to environmental allergens was also instructed.

After 2 weeks of treatment, erythema and purulent exudate in the left ear pinnae were alleviated. Also, neutrophils, macrophages



**FIGURE 2** | Open-mouth view radiography and computed tomography findings for a dog with otitis media. Lysis, density increase and irregular internal margin of the bilateral tympanic bulla wall were findings in the (a) open-mouth view radiography and (b) computed tomography (CT). (b) In CT, a mass of soft tissue density was identified in the left ear lesion (arrow). In addition, fluid in the bilateral tympanic bullae was observed in CT.



**FIGURE 3** | Photographs of the left ear condition. (a) Recurrence of abscess adjacent to left total ear canal ablation site. (b) Ear endoscopy revealed purulent material beside the eardrum. (c) Impression smear cytology revealed *Staphylococcus pseudintermedius* in the left tympanic bulla tissue.

and mild *Malassezia* infection were not observed on cytology. However, when dietary restriction and reduced exposure to environmental allergens were not controlled, an abscess recurred adjacent to the left TECA site (Figure 3a). Therefore, prednisolone (0.5 mg/kg PO BID; Solondo tab, Yuhan, Seoul, South Korea) was added to reduce severe inflammation. The abscess resolved while taking prednisolone, but recurred when prednisolone was tapered. On cytology of the recurred abscess obtained via FNA, many neutrophils and cocci were observed. The patient's pain response was severe and clinical symptoms such as exudate and pruritus worsened again, so a left bulla osteotomy was executed. During left bulla osteotomy, purulent material was confirmed beside the eardrum (Figure 3b). On cytology, cocci infection was confirmed on the tympanic bulla tissue (Figure 3c). In an antibiotic sensitivity test (Neodin Biovet. Laboratory, Seoul, South Korea), *Staphylococcus pseudintermedius* resistant to cephalosporin-based antibiotics was confirmed. Based on the antibiotic sensitivity results, antibiotics were changed from cefixime to marbofloxacin (5.5 mg/kg PO sid; Marbocyl tab, Vetoquinol Korea, Gyeonggi, South Korea). The resected tympanic bulla tissue showed fibrotic changes caused by chronic inflammation on histopathology (Figure 4a,b).

The patient presented with a recurrent abscess adjacent to the left TECA site 3 days after the left bulla osteotomy. Therefore, ASIT

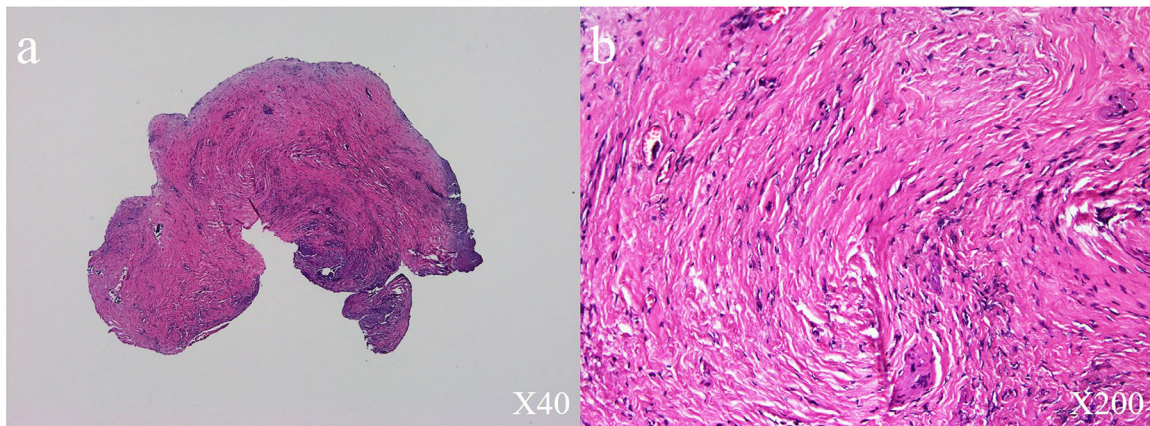
**TABLE 1** | Suggested dosage schedule for subcutaneous immunotherapy (Griffin and Hillier, 2001).

Week	1:100 w/v
1	0.1 mL
2	0.2 mL
3	0.3 mL
4	0.4 mL
5	0.5 mL
6	0.5 mL <sup>a</sup>
Continue with 0.5 mL every 10–21 days	

<sup>a</sup>Maintenance dose if tolerated; otherwise maintain at the highest to tolerated dose.

was started. The causative allergens were confirmed through an IgE serological test (Pobanilab, Gyeonggi, South Korea). Based on IgE serological testing, *Dermatophagoides pteronyssinus* and *Dermatophagoides farina* were selected. The ASIT schedule was planned by referring to Greer's suggested dosage schedule (Table 1) (Griffin and Hillier 2001). After ASIT, the head tilt was still present, but even though prednisolone was tapered and withdrawn over 2 months, the symptoms did not recur (Figure 5).





**FIGURE 4** | Histopathology of the left tympanic bulla tissue (a. 40× magnification, b. 200× magnification, H&E stain). (a) Connective tissue with inflammation. (b) Connective tissue is well differentiated and no malignant findings were observed.



**FIGURE 5** | The left ear after 10 months of allergen-specific immunotherapy (ASIT). The abscess adjacent to left TECA site was improved and did not recur after prednisolone withdrawal.

Currently, the patient is only being treated with ASIT over a year after antibiotic and antifungal agents were withdrawn and the condition of this patient is well managed without recurrence of symptoms.

### 3 | Discussion

This report describes a clinical case of canine refractory otitis media that was successfully treated with ASIT. Previous studies have reported that CAD is the most common primary risk factor of otitis externa and otitis media occurs secondarily in 50% to 80% of cases of chronic otitis externa (Cole et al. 1998; Little et al. 1991; Saridomichelakis et al. 2007). In the present case, at the time of diagnosis, the patient had no predisposing factors such as ears with excessive ear hair, stenotic ear canals and increased cerumen production in the canals. Primary factors include otic neoplasia, foreign body and otic parasites which were not found in radiography and dermatologic examination. On the basis of these results and the fulfilment of Favrot's criteria, the patient was diagnosed with otitis media caused by CAD.

Typical treatments for otitis media include topical therapy (e.g., topical glucocorticoids, topical antibacterial agents and topical antifungal agents), systemic therapy (e.g., glucocorticoids, immunosuppressive agents, antibiotics and antifungals) and surgery (e.g., bulla osteotomy and TECA) (Miller et al. 2013). In this patient, TECA surgery was performed three times at a local animal hospital, but there was no improvement. Therefore, ASIT, as a fundamental treatment, was performed and the treatment was successful.

This patient showed temporary improvement while using medications and restricting environmental factors. However, the abscess recurred when the medications were tapered. Medication therapy requires lifetime administration and only reduces clinical signs rather than reversing the pathogenesis (DeBoer 2017). Interestingly, ASIT is accomplished with minimal adverse effects and potential for long-lasting effectiveness, unlike medication therapy which has possible lifetime long-term adverse effects (DeBoer 2017). In ASIT, a switch from the canine T helper 2 (Th2) cell immune response to the T helper 1 (Th1) cell immune response has been demonstrated, with an increase in specific IgG concentrations and a decrease in specific IgE concentrations compared to the pre-treatment period (DeBoer et al. 2016). Environmental allergens induce Th2-polarized immune responses in CAD and this promotes the production and recruitment of inflammatory cells associated with hypersensitivity responses (Pucheu-Haston et al. 2015). Also, this response frequently leads to a secondary microbial infection of the affected skin (Hensel et al. 2015). Consequently, an allergic reaction not only induces otitis media but also increases infection susceptibility (Zernotti et al. 2017). Therefore, systemic desensitization was required to continuously maintain the temporary improvement of infection caused by medications in this case, so ASIT was introduced.

In humans, some clinical trials and reports of patient experience have highly encouraged the use of ASIT on otitis media, even in refractory cases (Choi et al. 2015; Di Rienzo et al. 2014; Novak 2007). In addition, successful treatment of refractory otitis media with ASIT in humans has been reported (Hurst 2008). The mechanisms by which ASIT works in dogs are parallel to those known in humans: early reduction of effector cell activities (eosinophils, basophils and mast cells) followed by a long-term

immunologic shift from a Th2 cell to a Th1 cell response and development of immunological tolerance (Akdis and Akdis 2015; Eifan et al. 2011; Mueller et al. 2018; Ozdemir et al. 2016). These shifts are accompanied by an increase in forkhead box P3 (FOXP3) + regulatory T cells (Tregs) and an increase in cytokines such as transforming growth factor-beta (TGFβ) and interleukin (IL)-10. Consequently, there is an increase in allergen-specific IgG and a decrease in allergen-specific IgE with extended treatment. In summary, ASIT induces immune tolerance to allergens, Tregs and regulatory B cells (Bregs) and increases allergen-specific IgG4 levels (Fennis et al. 2022; Głobińska et al. 2018; Palomares et al. 2017). ASIT decreases the IgE-to-IgG4 ratio and reduces the number of mast cells and eosinophils in the tissue and limits the release of their mediators as a long-term effect (Głobińska et al. 2018). In dogs, a shift to a Th1 cell response, an increase in IgG and IL-10 levels, and the appearance of more Treg cells have all been demonstrated (Fraser et al. 2004; Hou et al. 2008; Keppel et al. 2008; Shida et al. 2004). Thus, the ASIT mechanism in dogs is parallel to that of humans.

In addition, a *Malassezia* infection was observed on the left TECA lesion in this patient. *Malassezia* spp., lipophilic non-lipid-dependent yeasts, are normal microflora in the skin of healthy dogs, but they can become pathogens in conditions such as atopic dermatitis (Chen and Hill 2005). Acting as pathogens, *Malassezia* spp. cause IgE-mediated hypersensitivity and exacerbate the clinical symptoms of CAD (Scheynius et al. 2002; Sonesson et al. 2013). Impairment of the skin barrier caused by worsening of clinical symptoms leads to a progression of *Malassezia* infection and ASIT can prevent deterioration of clinical symptoms by reducing allergen-specific IgE (Głobińska et al. 2018; Sonesson et al. 2013). Also, there is a study in dogs that demonstrated ASIT allowed for a significant reduction in antifungal and anti-inflammatory therapy, which reduces the risk of pharmacological side effects (Åberg et al. 2017). ASIT can sometimes achieve a permanent cure (DeBoer 2017). Therefore, medications were able to be withdrawn in this patient after ASIT. Notably, the symptoms did not recur during a year follow-up period.

Neurologic signs of otitis media include facial nerve paresis or paralysis, Horner's syndrome and peripheral vestibular disease (e.g. head tilt, horizontal or rotary nystagmus, circling or falling toward the side of the lesion) (Nelson and Couto 2014; Platt and Olby 2013). This is because the facial nerve travels through the incomplete facial canal before exiting the stylomastoid foramen, and is exposed to the middle ear cavity (Platt and Olby 2013). When neurologic signs are present it may be permanent despite treatment (Nelson and Couto 2014). In this patient, the head tilt remained after treatment, which seems to be due to permanent vestibular (CN8) nerve damage.

There is a limitation in that ASIT was started after TECA surgery in this patient. Therefore it is unknown whether refractory otitis media can be successfully managed with ASIT without surgery. In addition, there is a lack of clear evidence of resolution because additional imaging was not re-performed after the improvement of the abscess. However, unlike before when symptoms recurred immediately after tapering of medication, long-term maintenance without recurrence suggests a therapeutic effect of ASIT. Nonetheless, this is the first case to show the effectiveness of ASIT in refractory otitis media in which previous medication therapy

and surgery were not effective. In conclusion, it will be helpful to consider ASIT as a major treatment option for refractory otitis media which has recurred even with long-term systemic or topical steroid therapy.

## 4 | Conclusion

This report showed that ASIT is a potential treatment for otitis media in which previous anti-inflammatory and antibiotic treatment was not effective. For successful management in dogs, the underlying cause of otitis media should be treated first rather than surgery.

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### Author Contributions

**Jihyun Kim:** data curation, formal analysis, investigation, software, visualization, writing – original draft, writing – review and editing data curation. **Ji-Hye Lee:** data curation, formal analysis, investigation, software, visualization, writing – original draft, writing – review and editing. **Yeji Kim:** data curation, formal analysis, investigation, software, visualization, writing – original draft, writing – review and editing data curation. **Yunji Song:** data curation, formal analysis, investigation, software, visualization, writing – original draft, writing – review and editing data curation. **Ha-Jung Kim:** conceptualization, funding acquisition, project administration, resources, supervision, validation, writing – review and editing.

### Ethics Statement

The authors have nothing to report.

### Conflicts of Interest

The authors declare no conflicts of interest.

### Data Availability Statement

The corresponding author will provide the datasets used and/or analysed during the current work upon reasonable request.

### Peer Review

The peer review history for this article is available at <https://publons.com/publon/10.1002/vms3.70253>.

### References

- Åberg, L., K. Varjonen, and S. Åhman. 2017. "Results of Allergen-Specific Immunotherapy in Atopic Dogs With *Malassezia* Hypersensitivity: A Retrospective Study of 16 Cases." *Veterinary Dermatology* 28: 633–e157.
- Akdis, C. A., and M. Akdis. 2015. "Mechanisms of Allergen-Specific Immunotherapy and Immune Tolerance to Allergens." *World Allergy Organization Journal* 8: 17.
- Bajwa, J. 2019. "Canine Otitis Externa—Treatment and Complications." *Canadian Veterinary Journal* 60: 97–99.
- Chen, T. A., and P. B. Hill. 2005. "The Biology of *Malassezia* Organisms and Their Ability to Induce Immune Responses and Skin Disease." *Veterinary Dermatology* 16: 4–26.
- Choi, J. S., H. R. Ryu, C. H. Yoon, et al. 2015. "Treatment of Patients With Refractory Atopic Dermatitis Sensitized to House Dust Mites by Using Sublingual Allergen Immunotherapy." *Annals of Dermatology* 27: 82–86.
- Cole, L. K., K. W. Kwochka, J. J. Kowalski, and A. Hillier. 1998. "Microbial Flora and Antimicrobial Susceptibility Patterns of Isolated Pathogens



- From the Horizontal Ear Canal and Middle Ear in Dogs With Otitis Media." *Journal of the American Veterinary Medical Association* 212: 534–538.
- DeBoer, D. J. 2017. "The Future of Immunotherapy for Canine Atopic Dermatitis: A Review." *Veterinary Dermatology* 28: 25–e6.
- DeBoer, D. J., M. Verbrugge, and M. Morris. 2016. "Clinical and Immunological Responses of Dust Mite Sensitive, Atopic Dogs to Treatment With Sublingual Immunotherapy (SLIT)." *Veterinary Dermatology* 27: 82–e24.
- Di Rienzo, V., G. Cadario, T. Grieco, et al. 2014. "Sublingual Immunotherapy in Mite-Sensitized Children With Atopic Dermatitis: A Randomized, Open, Parallel-Group Study." *Annals of Allergy, Asthma & Immunology* 113: 671–673.e1.
- Eifan, A. O., M. H. Shamji, and S. R. Durham. 2011. "Long-Term Clinical and Immunological Effects of Allergen Immunotherapy." *Current Opinion in Allergy and Clinical Immunology* 11: 586–593.
- Eisenschenk, M. C., P. Hensel, M. N. Saridomichelakis, C. Tamamoto-Mochizuki, C. M. Pucheu-Haston, and D. Santoro. 2024. "Introduction to the ICADA 2023 Canine Atopic Dermatitis Pathogenesis Review Articles and Updated Definition." *Veterinary Dermatology* 35, no. 1: 3–4.
- Fennis, E. E. M., C. M. M. van Damme, Y. M. Schlotter, et al. 2022. "Efficacy of Subcutaneous Allergen Immunotherapy in Atopic Dogs: A Retrospective Study of 664 Cases." *Veterinary Dermatology* 33, no. 4: 321–e75.
- Fraser, M. A., P. E. McNeil, and G. Gettinby. 2004. "Examination of Serum Total IgG1 Concentration in Atopic and Non-Atopic Dogs." *Journal of Small Animal Practice* 45: 186–190.
- Głobińska, A., T. Boonpiyathad, P. Satitsuksanoa, et al. 2018. "Mechanisms of Allergen-Specific Immunotherapy: Diverse Mechanisms of Immune Tolerance to Allergens." *Annals of Allergy, Asthma & Immunology* 121: 306–312.
- Gotthelf, L. N. 2004. "Diagnosis and Treatment of Otitis Media in Dogs and Cats." *Veterinary Clinics of North America. Small Animal Practice* 34: 469–487.
- Grammar, L. C., and P. A. Greenberger. 2018. "Principles of Immunologic Management of Allergic Diseases due to Extrinsic Antigens." In *Patter-son's Allergic Diseases*, edited by L. C. Grammar, and K. E. Harris, 515–536. Wolters Kluwer.
- Griffin, C. E., and A. Hillier. 2001. "The ACVD Task Force on Canine Atopic Dermatitis (XXIV): Allergen-Specific Immunotherapy." *Veterinary Immunology and Immunopathology* 81: 363–383.
- Hensel, P., D. Santoro, C. Favrot, P. Hill, and C. Griffin. 2015. "Canine Atopic Dermatitis: Detailed Guidelines for Diagnosis and Allergen Identification." *BMC Veterinary Research* 11: 196.
- Hou, C. C., C. E. Griffin, and P. B. Hill. 2008. "Dermatophagoides Farinae-Specific IgG Responses in Atopic Dogs Undergoing Allergen-Specific Immunotherapy With Aqueous Vaccines." *Veterinary Dermatology* 19: 215–220.
- Hurst, D. S. 2008. "Efficacy of Allergy Immunotherapy as a Treatment for Patients With Chronic Otitis Media With Effusion." *International Journal of Pediatric Otorhinolaryngology* 72: 1215–1223.
- Keppel, K. E., K. L. Campbell, F. A. Zuckermann, E. A. Greeley, D. J. Schaeffer, and R. J. Husmann. 2008. "Quantitation of Canine Regulatory T Cell Populations, Serum Interleukin-10 and Allergen-Specific IgE Concentrations in Healthy Control Dogs and Canine Atopic Dermatitis Patients Receiving Allergen-Specific Immunotherapy." *Veterinary Immunology and Immunopathology* 123: 337–344.
- Kern, T. J., and H. N. Erb. 1987. "Facial Neuropathy in Dogs and Cats: 95 Cases (1975–1985)." *Journal of the American Veterinary Medical Association* 191: 1604–1609.
- La Mantia, I., A. Varricchio, and G. Ciprandi. 2021. "Allergen Immunotherapy in Children With Otitis media With Effusion: A Preliminary Experience." *European Annals of Allergy and Clinical Immunology* 53: 288–290.
- Little, C. J., J. G. Lane, and G. R. Pearson. 1991. "Inflammatory Middle Ear Disease of the Dog: The Pathology of Otitis Media." *Veterinary Record* 128: 293–296.
- Miller, W. H., C. E. Griffin, and K. L. Campbell. 2013. "Diseases of Eyelids, Claws, Anal Sacs, and Ears." In *Small Animal Dermatology*, edited by M. B. Glaze, 741–773. 7th ed. Elsevier.
- Moote, W., and H. Kim. 2011. "Allergen-Specific Immunotherapy." *Allergy, Asthma, and Clinical Immunology* 7, no. Suppl 1: S5.
- Mueller, R. S., E. Jensen-Jarolim, F. Roth-Walter, et al. 2018. "Allergen Immunotherapy in People, Dogs, Cats and Horses—differences, Similarities and Research Needs." *Allergy* 73, no. 10: 1989–1999.
- Nelson, R. W., and C. G. Couto. 2014. "Head Tilt." In *Small Animal Internal Medicine*, edited by S. M. Taylor, 1028–1035. 5th ed. Elsevier.
- Novak, N. 2007. "Allergen Specific Immunotherapy for Atopic Dermatitis." *Current Opinion in Allergy and Clinical Immunology* 7: 542–546.
- Olivry, T., D. J. DeBoer, C. Favrot, et al. 2010. "Treatment of Canine Atopic Dermatitis: 2010 Clinical Practice Guidelines From the International Task Force on Canine Atopic Dermatitis." *Veterinary Dermatology* 21: 233–248.
- Ozdemir, C., U. C. Kucuksezer, M. Akdis, and C. A. Akdis. 2016. "Mechanisms of Aeroallergen Immunotherapy: Subcutaneous Immunotherapy and Sublingual Immunotherapy." *Immunology and Allergy Clinics of North America* 36: 71–86.
- Palomares, O., M. Akdis, M. Martín-Fontecha, and C. A. Akdis. 2017. "Mechanisms of Immune Regulation in Allergic Diseases: The Role of Regulatory T and B Cells." *Immunological Reviews* 278: 219–236.
- Platt, S. R., and N. J. Olby. 2013. "Head Tilt and Nystagmus." In *BSAVA Manual of Canine and Feline Neurology*, edited by K. R. Munana, 195–212. 4th ed. Blackwell Publishers.
- Pucheu-Haston, C. M., P. Bizikova, R. Marsella, D. Santoro, T. Nuttall, and M. N. Eisenschenk. 2015. "Review: Lymphocytes, Cytokines, Chemokines and the T-Helper 1-T-Helper 2 Balance in Canine Atopic Dermatitis." *Veterinary Dermatology* 26, no. 2: 124–e32.
- Saridomichelakis, M. N., R. Farmaki, L. S. Leontides, and A. F. Koutinas. 2007. "Aetiology of Canine Otitis Externa: A Retrospective Study of 100 Cases." *Veterinary Dermatology* 18: 341–347.
- Scheynius, A., C. Johansson, E. Buentke, A. Zargari, and M. T. Linder. 2002. "Atopic Eczema/Dermatitis Syndrome and Malassezia." *International Archives of Allergy and Immunology* 127: 161–169.
- Shida, M., M. Kadoya, S. J. Park, K. Nishifuji, Y. Momoi, and T. Iwasaki. 2004. "Allergen-Specific Immunotherapy Induces Th1 Shift in Dogs With Atopic Dermatitis." *Veterinary Immunology and Immunopathology* 102: 19–31.
- Sonesson, A., J. Bartosik, J. Christiansen, et al. 2013. "Sensitization to Skin-Associated Microorganisms in Adult Patients With Atopic Dermatitis Is of Importance for Disease Severity." *Acta Dermato-Venereologica* 93: 340–345.
- Zernotti, M. E., R. Pawankar, I. Ansotegui, et al. 2017. "Otitis Media With Effusion and Atopy: Is There a Causal Relationship?." *The World Allergy Organization Journal* 10: 37.