



PEER REVIEWED

VITAL VACCINATION SERIES

VACCINE ADVERSE EVENTS

Acute Allergic Angioedema

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A vaccine adverse event (adverse reaction) is defined as: *any undesirable side effect or unintended effect (including failure to immunize) associated with the administration of a licensed biologic product (vaccine).*¹

While the actual incidence of vaccine-associated adverse reactions in veterinary medicine is considered to be low, studies addressing the pathophysiology, management, and prevention of vaccine adverse events in veterinary medicine are limited.^{2,3}

ANGIOEDEMA DEFINED

Of the acute vaccine adverse events known to occur in cats and dogs, post-vaccinal angioedema, or swelling of the face and ears, appears to be among the most common adverse events observed and treated in practice.⁴

Pathophysiology

In dogs and cats, post-vaccination angioedema is believed to result from a type-1 hypersensitivity and IgE-mediated degranulation of mast cells in skin.⁵

Potent vasoactive compounds—such as histamine, platelet activating factor, leukotrienes, and prostaglandin D₂—cause fluid release in the following (deeper) layers of skin:

- Dermis
- Mucosa
- Submucosa.

These compounds are likely responsible for the development of post-vaccinal angioedema.

Angioedema is distinguished from urticaria (or hives), an acute pruritic allergic reaction, due to the fact that urticaria affects the superficial

layers of skin. Respiratory distress (laryngeal edema) is occasionally reported in humans with acute-onset angioedema but has not been reported in dogs or cats.

Clinical Signs

The periorbital tissues and muzzle are commonly affected (**Figure**). Affected animals typically develop localized (versus systemic) asymmetrical swelling of the skin and mucous membranes within minutes to a few hours following administration of a vaccine.

Limited studies in affected dogs indicate that vital signs and laboratory profiles tend to be normal. Although some animals may appear to manifest mild discomfort associated with the swelling, pruritus is uncommon.

Incidence

The true incidence of post-vaccination angioedema is unknown due to limited reporting and the absence of a



Figure. Post-vaccinal angioedema in a dachshund

Vist bevaccinesmart.com—a website that offers vital information for both veterinarians and pet owners—to find comprehensive coverage on the importance of vaccination, history and perception of vaccines, clinical signs to watch for after vaccination, resources practitioners can use within their practices, and much more.

meaningful, accessible adverse event database for veterinary medicine. Lack of data further complicates the compilation of key epidemiologic information, such as type of vaccine(s) administered, prior vaccination history, patient age, breed, and gender, which could facilitate efforts by veterinarians to reduce reactions or mitigate risk during subsequent vaccine appointments.



Urticaria (hives) and pruritus are not commonly associated with post-vaccinal angioedema.

VACCINE-INDUCED ANGIOEDEMA

Vaccine Type

While acute-onset angioedema is *anecdotally* reported to be associated with administration of leptospirosis vaccines, the reaction has occurred in dogs that have never received a dose of leptospirosis vaccine. In addition, similar post-vaccinal reactions have been observed in cats. Inactivated vaccines, such as rabies and Lyme borreliosis, as well as attenuated (modified-live) vaccines have been implicated.

Antigen Role

The specific antigen(s) responsible for causing acute angioedema may not, in fact, be associated with the immunizing antigen. Excipient proteins and associated chemicals typically found in many vaccines (eg, bovine serum albumin, adjuvant, antibiotic) may act as a sensitizing allergen in an individual animal. For this reason, simply changing vaccine manufacturers does not guarantee that the reaction will not reoccur in a patient with a prior history of angioedema.

RISK FACTORS

Dogs

Risk factors reported to be associated with acute onset (within 72 hours) post-vaccinal reactions suggest a greater risk among young adult, small-breed (≤ 10 kg), neutered dogs that receive multiple vaccine doses at the same appointment.⁶

Cats

Risk factors for cats are similar and suggest that post-vaccinal (occurring within 30 days) adverse reactions were most likely to occur in young adult, neutered cats that receive multiple vaccine doses at the same appointment.⁷ However, these studies assessed the occurrence of multiple types of adverse reactions and were not limited to angioedema.

Revaccination

Interestingly, there are no studies documenting increased risk for adverse reactions at the time of revaccination among patients with a prior history of post-vaccinal angioedema.

IN BRIEF

Vaccine Adverse Reaction: Acute Allergic Angioedema

Clinical Signs	<ul style="list-style-type: none"> Localized, nonpruritic, asymmetrical swelling of the skin/mucous membranes of the periorbital tissues Within minutes to a few hours following administration of a vaccine
Risk Factors	<p>Dogs</p> <ul style="list-style-type: none"> Associated with acute onset (within 72 H) post-vaccinal reactions Young adult, small-breed neutered dogs receiving multiple vaccines at same appointment <p>Cats</p> <ul style="list-style-type: none"> Associated with post-vaccinal (occurring within 30 days) adverse reactions Young adult, neutered cats receiving multiple vaccines at same appointment
Treatment	<ul style="list-style-type: none"> Prednisolone, 0.5 to 1 mg/kg IM or IV (single dose) Hospitalize patient and observe for 1 to 2 H If complicated angioedema, treat with IV fluids and epinephrine
Prevention	<p>Patients with prior history of post-vaccinal angioedema:</p> <ul style="list-style-type: none"> Dogs: Diphenhydramine, 2 to 4 mg/kg PO or 1 to 2 mg/kg IM 30 min before vaccination Cats: Diphenhydramine, 2 to 4 mg/kg PO or 1 mg/kg IM 30 min before vaccination

PATIENT MANAGEMENT

The clinician should consider 2 issues regarding the management of acute-onset post-vaccination angioedema:

1. Immediate treatment of the affected patient
2. Preventive measures for patients with a prior history of post-vaccinal angioedema.

Immediate Treatment of Affected Patient

Because it is not possible to predict which patients will have mild, self-limiting signs and which ones will develop severe swelling or systemic anaphylaxis, treatment of any patient with evidence of post-vaccinal edema is justified.

- Parenteral (IM or IV) administration of a single dose of **prednisolone, 0.5 to 1 mg/kg**, is expected to be sufficient.
- Ideally, the patient should be hospitalized and observed for at least 1 to 2 hours to determine if the signs worsen or respiratory distress develops.



This is the third article in Dr. Richard Ford's **Vital Vaccination Series**. Read the previous two articles at todaysveterinarypractice.com.

- **Canine Vaccination Guidelines: Key Points for Veterinary Practice** (Sept/Oct 2012)
- **Dogs & Cats Overdue for Vaccination: Recommendations for Updating Immunizations** (Nov/Dec 2012)

- Administration of an antihistamine, such as diphenhydramine, is not contraindicated. However, a patient is unlikely to benefit significantly from a dose of an H-1 inhibitor once histamine has been released and tissue swelling has developed.
- Treatment with IV fluids and epinephrine is not indicated in the patient with uncomplicated angioedema.

Patient with Prior History of Post-Vaccinal Angioedema

Although vaccination of patients with a prior history of angioedema is not contraindicated, the clinician should attempt to limit the number of vaccines administered to only those deemed necessary. Note that arbitrarily reducing the volume of a vaccine dose to mitigate risk may result in failure to immunize and, therefore, is NOT recommended.¹

In addition, many clinicians elect to administer treatment prior to vaccination to mitigate potential risk associated with revaccination; however, the benefits an individual patient derives from pre-vaccination treatment have not been studied.

Pre-vaccination treatment typically entails:

- **Dogs:** Administration of a single dose of **diphenhydramine, 2 to 4 mg/kg PO or 1 to 2 mg/kg IM** (maximum dose, 50 mg), approximately 30 minutes prior to vaccination
- **Cats:** Administration of a single dose of **diphenhydramine, 2 to 4 mg/kg PO or 1 mg/kg IM**.
- IV administration of diphenhydramine is NOT recommended in these patients.

Anecdotally, some practices recommend administering both an antihistamine and corticosteroid prior to revaccination. ■

References

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5. Moore GE, HogenEsch H. Adverse vaccinal events in dogs and cats. *Vet Clin Small Anim Small Anim Pract* 2010; 40:393-407.
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REPORTING VACCINE ADVERSE EVENTS

Although reporting of vaccine adverse events in the U.S. and Canada is voluntary, veterinarians are encouraged to report known and suspected adverse reactions.

In the United States

Veterinarians are encouraged to report vaccine adverse events to the Technical Services section of the manufacturer of the product(s) suspected to have caused the reaction prior to contacting the regulatory agency, the USDA Center for Veterinary Biologics (CVB).

Alternatively, veterinarians may contact the CVB directly; 3 options are available:

- **Online:** www.aphis.usda.gov/animal_health/vet_biologics/vb_adverse_event.shtml
- **Fax or mail:** Download PDF form from CVB web-site and:
 - » Fax to 515-337-6120 or
 - » Mail to the CVB at 1920 Dayton Ave, PO Box 844, Ames IA 50010
- **Phone:** Call the CVB at 800-752-6255

In Canada

Veterinarians are encouraged to contact the manufacturer of the product(s) believed to have caused the adverse event.

Alternatively, veterinarians can report a vaccine adverse event to the Canadian Food Inspection Agency (CFIA) by accessing Form CFIA/ACIA 2205: Notification of Suspected Adverse Events to Veterinary Biologics, available at <http://inspection.gc.ca/english/for/pdf/c2205e.pdf>.



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