

Epidemiological Review of Insect Sting Allergy in Naval Aviation: Current Policy and Real-World Practices

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Individuals with conditions not addressed in the physical standards section of the Navy's Manual of the Medical Department can be considered for a waiver that would allow them to continue in naval aviation. Insect sting allergy is addressed in the Navy's waiver guide; however, the actual disposition of these individuals does not coincide with published waiver policies. Our objective was to identify discrepancies, to review current clinical guidelines, and to offer recommendations for updating the Navy's waiver policy. Aviation medical records of individuals with insect sting allergies from 1985 to 2002 were reviewed. Disposition, waiver status, and allergy evaluation were investigated. The data suggest that waiver requests have been addressed not under the current waiver guidelines but instead under current clinical guidelines. New guidelines that properly reflect current diagnostic and treatment modalities were voted on by the Aeromedical Advisory Council and submitted to the Navy's Bureau of Medicine. These changes were incorporated into the Navy's aviation waiver policy guidelines.

Introduction

The risks posed by sting allergies in aviation encompass more than just possible death. Anaphylaxis resulting in a potentially lethal catastrophe is of great concern, especially for single-seat aircraft or aircraft flying near populated areas. In 1999, a case review in the *Journal of Aviation, Space, and Environmental Medicine* described an allergic reaction of an aviator within 30 minutes after landing. The patient became dizzy, syncopal, incapacitated, and incontinent. Initially his condition was thought to be from new-onset seizure activity or an arrhythmia. However, after a complete evaluation, he was found to have experienced an anaphylactic reaction to a bee sting.¹ In fact, incapacitation from an allergic reaction can occur in <5 minutes.

According to the Navy's aviation waiver guide, published and maintained by the Aeromedical Qualifications Department (Code 342), any individual with a history of insect sting allergies is physically disqualified from aviation duty in the Navy. Naval aviation includes pilots, naval flight officers, air traffic controllers, maintenance personnel, and unmanned vehicle operators. Individuals may request a waiver for this condition once they are receiving a stable dose of venom immunotherapy (VIT). The guide states, "Someone who has completed a course of desensitization and has no reaction to a challenge dose is quite likely to be waived even with anaphylaxis history."² In addition, the waiver guide states that waivers are not appropriate for any member who is at such risk that he or she is advised to carry an emergency adrenaline kit.

The purpose of our research was to identify discrepancies

between the Navy's published waiver policies and practices. Once any discrepancies were identified, current clinical guidelines were reviewed and recommendations for changes to the waiver guide were presented before the Navy Aeromedical Advisory Council (AAC) for final disposition.

Background

Each year in the United States, 40 to 50 individuals succumb to the fatal effects of anaphylaxis caused by insect sting allergies.³ The culprits are hymenopterans and imported fire ants (IFAs), which are particularly prevalent in the southeast region of the nation. The order Hymenoptera includes the vespids (wasps and hornets), the apids (honey bees and bumble bees), and the formicids (IFAs). Yellow jackets, also from the family Vespidae, are ground-dwelling insects. They are extremely aggressive and sting with very little provocation. They are the primary stinging culprit in North America.⁴ The hornets of concern are the yellow hornet and the white-faced hornet. These are aerial nesting yellow jackets and not true hornets. They are sensitive to vibration and usually sting only when their nests are disturbed. They are often found near garbage and rotten fruit, where they feed. Wasps build honeycomb nests, usually in dark areas such as under eaves or porches of homes. They are reddish orange in color and are less aggressive than hornets or yellow jackets. Honeybees tend to nest in tree hollows or old logs. They are usually not very aggressive away from the hive. They leave a barbed stinger with an attached venom sack, which is pathognomonic for a honeybee sting.

IFAs are identified as the most common insect sting or bite allergy in our research population. Since arriving in North America in the early 1900s through the port of Mobile, Alabama, they have successfully migrated throughout the majority of the southeast and are slowly moving west and north. They build large mounds of fresh soil and are very aggressive if their mounds are disturbed. IFAs can both bite and sting. They bite through the skin with their mandibles and use this as an anchoring pivot point as they rotate and sting multiple times in a circular pattern. With each sting, a sterile pustule develops within 24 hours, which is pathognomonic for an IFA sting.

The average individual in the general population has a 2% to 3% risk of a systemic reaction to an insect sting. Forty percent to 80% of insect sting fatalities occur among individuals with no history of previous sting.⁵ Unfortunately, there are no valuable screening tests that can predict who will have a systemic or anaphylactic reaction to an insect sting or bite. However, individuals who have experienced a systemic reaction have a 60% chance of sustaining another systemic reaction with their next sting, a risk ~30 times greater than that of the general population.⁶

The insect sting allergic response is an IgE-mediated type 1 hypersensitivity reaction. There are two types of reactions, i.e.,

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cutaneous only, with urticaria and angioedema, and systemic, ranging from bronchospasm and laryngeal edema to hypotension, shock, and death. Sting allergies may also be the etiological agent in such conditions as serum sickness, vasculitis, and periarthritis nodosum and can cause gastrointestinal upset and necrotic inflammatory granulomatous lesions. In addition, with multiple stings a toxic anaphylactoid reaction can occur that is not IgE mediated.⁷

Sensitization occurs for 30% of adults within the first 1 month after an exposure.⁸ Skin test sensitivity decreases at an approximate rate of 10% to 12% per year. Ten percent of those individuals still have a positive skin test >3 years after their last exposure. A common misunderstanding is that your next sting may well be your last, because of increasing sensitivity to the allergen. In fact, clinical observations have shown that a patient's systemic reaction is quite stable and, with no intervention, will most likely be very similar to the reaction experienced previously.¹ Individuals with a history consistent with insect sting allergies or those being considered for VIT should be referred for skin testing. All individuals who have had a systemic reaction or a large local reaction where systemic response cannot be sufficiently ruled out are candidates for VIT. However, if skin testing is negative, regardless of the patient's history or age, then VIT is usually not indicated (Table I). In some instances, if the history is compelling and the skin test is negative, a radioallergen sorbent test (RAST) is performed. Although RAST is a direct serum measurement of IgE, there are numerous other conditions that can cause elevated serum IgE levels. Therefore, there is no evidence to suggest that RAST is more reliable or diagnostic than skin testing.⁵ Thus, a positive RAST is not indicative of insect sting allergy. With a positive RAST, a negative skin test, and a positive history, an individual has a 40% risk of sustaining a systemic reaction with his or her next exposure.⁹ With a positive skin test and no reported history of sting exposure, an individual has a 17% chance of systemic reaction with a sting or bite exposure, which is approximately 6 times that of the general population.⁵ Unfortunately, skin testing and RAST are not reliable screening tools. Our best clinical marker, the skin test, has a positive predictive value of only 50% with a positive history.⁹ Therefore, without a positive history, there is no indication for VIT or any other treatment modality.

VIT consists of a number of initial injections to desensitize the individual, followed by maintenance injections every 6 to 8 weeks.¹⁰ There is some evidence that even longer intervals (up to 12 weeks) between maintenance doses may be effective. The initial VIT can be performed over weeks or in 1 day, which is

TABLE I
INDICATIONS FOR VIT

History	Skin Test Results	RAST Results	Treatment
+	+	NA	VIT
-	+	NA	No VIT
+	-	+	Uncertain

When a positive history is followed by a positive skin test, VIT is indicated. VIT is not indicated when there is no history of sting allergy present, regardless of skin test results or RAST results. When the history is positive, the skin test is negative, and the RAST is positive, there is clinical uncertainty regarding the appropriateness of VIT. NA, not applicable.

known as rush VIT and is equally effective.¹¹ Rush VIT limits degradation in operational readiness by expeditiously and safely returning aviators to flight status. The effectiveness of VIT is characterized by the fact that it prevents systemic reactions to insect stings 97% of the time.⁶ Therefore, immediately after VIT, the risk of systemic reaction with a subsequent exposure is 2% to 5%, almost exactly equal to the risk of the general population⁶ (Fig. 1). Those who do suffer subsequent reactions seem to have reactions much less severe than their initial reaction.

IFA venom is not available for clinical use. Instead, the whole-body extract seems to contain the relevant allergens. Immunotherapy with IFA whole-body extract appears to be protective for approximately 80% to 88% of individuals, somewhat less than VIT with venom extract.¹⁰ Also, skin reactivity seems to be a poor indicator of the risk for a systemic reaction to IFA stings after IFA immunotherapy.

Methods

The Navy Bureau of Medicine (BUMED) and Code 342 initiated this research after they determined the need for waiver guideline revisions concerning insect sting allergy. These Navy departments are responsible for determining the medical issues in need of review because of outdated waiver policies, current clinical guideline changes, or complications arising from past policies. These topics are then assigned to the Residents in Aerospace Medicine at the Naval Aerospace Medical Institute in Pensacola, Florida, who initiate detailed research and analysis of the assigned topic. Subsequently, Residents in Aerospace Medicine present their research findings and recommendations to the AAC, which votes on the recommendations after thorough review. The results are sent to BUMED for final endorsement.

We reviewed all applicable aviation medical waiver requests available through the database at the Naval Aerospace Medical Institute Code 342. Records dating back to 1985 were queried using International Classification of Diseases, 9th Revision, Clinical Modification codes 989.5 (toxic effect venom), 995.0 (anaphylaxis), and 995.3 (unspecified allergy). One hundred eighty-two useful records were identified and reviewed in their entirety. Information concerning patients' history, treatment, flight status, and waiver status was recorded. Descriptive statistics were used to organize and review the information. The final results were presented to the AAC for discussion and a final vote. The current waiver guide is updated once the AAC's vote receives endorsement by BUMED. Policies are changed and updated based on current literature describing the epidemiology, natural history, treatment options, and treatment outcomes of sting allergies and, finally, how these factors affect the specific environment of naval aviation. Code 342 then posts the applicable changes in the Navy's waiver guide. Results of this process ensure that the Navy's aviation waiver policy is continuously updated to meet the ever-changing clinical management guidelines and the flight environment.

Results

All records matching International Classification of Diseases, 9th Revision, Clinical Modification codes from the query were reviewed in their entirety. Of those 196 matching records, 14 were miscoded and 17 were not found. The 14 miscoded records

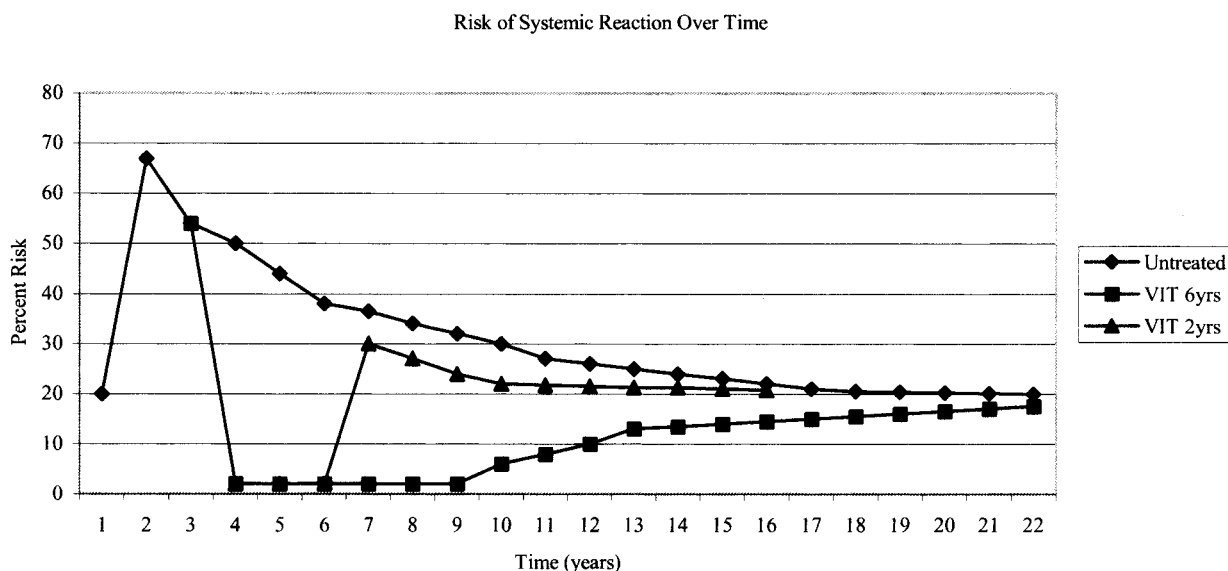


Fig. 1. Natural history of insect stings over time, in 1-year increments. The top line (diamonds) demonstrates that a person's risk of systemic reaction after an insect sting can peak between 60% and 70% with a previous history of systemic reaction to a sting. This risk slowly dissipates over time, leveling off at approximately 18% to 22% risk of systemic reaction with the next sting at 15 years. The middle line (triangles) demonstrates the effects on the risk of systemic reaction with the next sting with only 2 years of VIT. With only 2 years of VIT, the risk-reduction benefit is quickly lost with the discontinuation of VIT. This demonstrates the necessity and the standard of care of a minimum of 3 years of VIT to maintain the risk-reduction benefit of VIT. The bottom line (squares) shows the effect of VIT started arbitrarily 2 years after a positive history of a systemic reaction to an insect sting. It is evident that risk immediately falls to 2% to 5% that of the general population. After completion of 6 years of VIT, the protective effect slowly decreases until individual risk reaches 15% to 18%, the same risk after 15 years as that of individuals who never received VIT.

were not applicable and were removed from the analysis. Pertinent data were extracted from the other 17 query reports. Therefore, the complete records for 165 aviators were reviewed and 17 documents with valuable waiver data but limited medical information were also included, for a total of 182 records in the analysis. Of the 182 records, 119 aviators (65%) were granted a waiver for their sting allergy or hypersensitivity. The other 64 (35%) were denied a waiver. Interestingly, aircrew candidates and aircrew members, who never have actual control of the

aircraft, were most often denied waivers, almost 50% of the time (Fig. 2). Individuals reporting anaphylactic reactions more severe than a systemic cutaneous reaction were more often denied a waiver. With a recorded anaphylactic reaction, waivers were granted 65% of the time. However, when the reaction was reported as a systemic cutaneous reaction, waivers were granted 78% of the time (Fig. 3).

Only 15% of all individuals considered for a waiver had a documented prescription for a prophylactic adrenaline emergency kit. A

Aviation Category Distribution Among Waiver Applicants

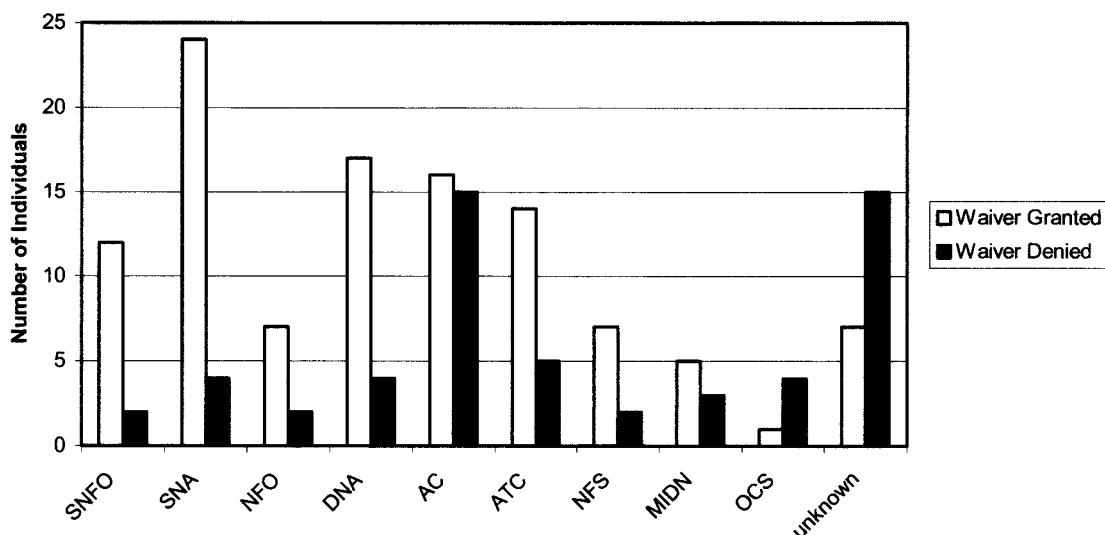


Fig. 2. Waiver disposition by aviation category. Aircrew was the single group most often denied a waiver. Aircrew members never have actual control of the aircraft in flight. SNFO, student naval flight officer; SNA, student naval aviator; NFO, naval flight officer; DNA, designated naval aviator; AC, aircrew; ATC, air traffic controller; NFS, naval flight surgeon; MIDN, midshipman; OCS, officer candidate school.

Waiver Approval by Individual Allergy Response

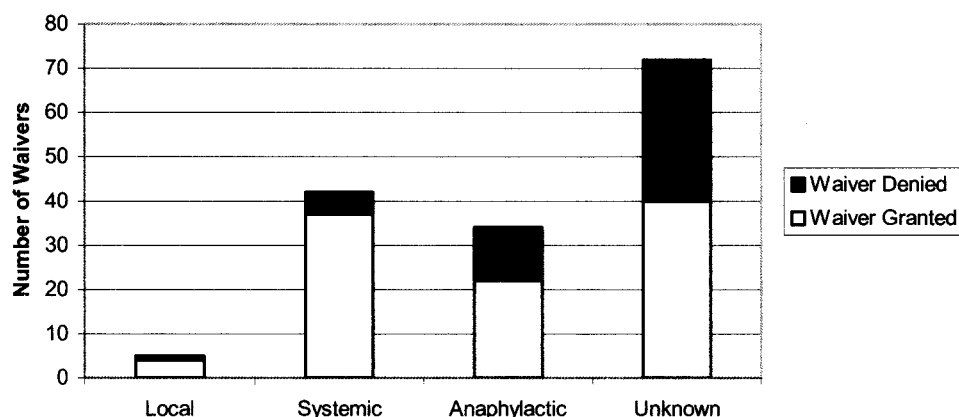


Fig. 3. Waiver approval by individual allergy response. Systemic reactions were categorized to differentiate between cutaneous systemic reactions and anaphylactic reactions with organ involvement (shock, respiratory compromise, and gastrointestinal distress). Anaphylactic reactions were less likely to receive waivers, as might be expected. Sixty-five percent of individuals with anaphylactic allergic responses were granted waivers for their conditions. Eighty-eight percent with only systemic cutaneous reactions were granted waivers. Eighty percent of individuals with only local reactions received waivers.

number of the allergists' reports specified that the individual would no longer need to carry the emergency adrenaline kit after VIT. Of the 25 patients who were prescribed emergency kits, 65% were granted waivers for their condition and 35% were denied. According to the records, all aviation candidates, regardless of the severity of their sting allergy or the age at which they had the reaction, were required to complete desensitization and 3 years of maintenance VIT before being granted a waiver.

Discussion

After reviewing and analyzing the data, it was clear that the Navy's decisions regarding sting allergy waivers were not accurately represented in the Navy's waiver guide. These inconsistencies were presented to and reviewed by the AAC, and recommended policy changes were voted on. The three issues put forth to the AAC were as follows: (1) whether emergency adrenaline prescription should serve as grounds for waiver denial, (2) disposition of aviation candidates with a history of systemic reaction before the age of 16, and (3) disposition of aviation candidates with a history of sting allergy before entrance into naval aviation, compared with already designated aviation personnel.

First, it is clear that being prescribed emergency adrenaline does not negatively affect one's waiver request (Fig. 4). It is also questionable whether all emergency anaphylactic kits prescribed were actually documented. That is, according to the records reviewed, only 15% of patients with sting allergies were ever given these kits. Generally, for medical and legal reasons, emergency adrenaline is given to most, if not all, patients who have experienced a systemic or anaphylactic response to a sting. It is well established in the literature that a "... delay in the recognition of severe anaphylaxis and subsequent administration of epinephrine has been reported to be the principle contributor to poor outcome and mortality. Predictors of poor outcome include patients with asthma and individuals with a history of previously life-threatening anaphylactic episode. Consequently, the immediate availability of epinephrine injections is paramount for survival."⁴ Therefore, it is quite possible that

Waiver Determination for Those Prescribed Adrenaline

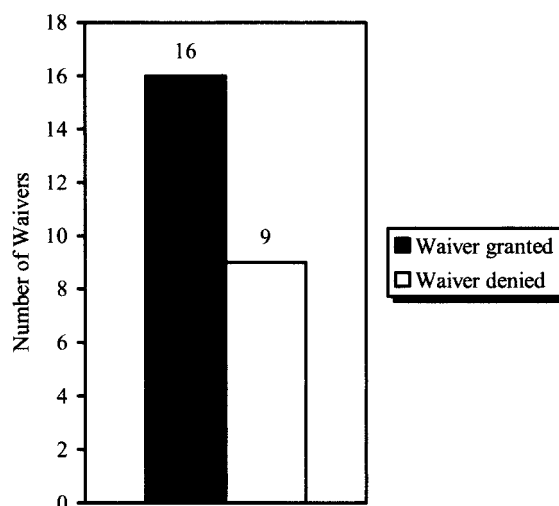


Fig. 4. Waiver determination for subjects prescribed emergency adrenaline kits. Having been prescribed emergency adrenaline for sting allergies did not negatively affect the granting of a waiver. In fact, subjects prescribed adrenaline were more likely to be granted waivers, although the Navy waiver guide specifically states that being prescribed emergency adrenaline is grounds for denial of a waiver.

under-reporting exists because of the absoluteness of the waiver guide's stated denial of a waiver with an emergency adrenaline kit prescription. However, from the analysis it was clear that 65% of those prescribed emergency adrenaline received a waiver for duty involving flying. Consequently, the AAC voted that having been prescribed emergency adrenaline would not affect an individual's eligibility for a waiver. Additionally, in certain cases where an individual's reaction was life-threatening or the airway was compromised, it would be mandatory to have emergency adrenaline available during flight. This mandate would be clearly written into the body of the waiver.

Second, it is well established in the literature that children can quite simply "outgrow" their sting allergy and not have a systemic response as an adult. In fact, the current clinical recommendation is that individuals ≤ 16 years of age who have had a cutaneous systemic reaction or mild anaphylactic reaction with organ involvement are not necessarily candidates for VIT. Only after a patient experiences a more severe reaction at a young age is it recommended that the physician, parents, and patient discuss the necessity, risks, and benefits of VIT.⁵ However, these specific situations are not currently addressed in the Navy's waiver guide. Therefore, in agreement with current medical guidelines, it was voted that patients who experienced insect sting allergies at ≤ 16 years of age would not be required to go for skin testing if their history supported a cutaneous systemic reaction. However, where current recommendations offer choice and uncertainty with respect to those ≤ 16 years of age who experience a more severe reaction, the AAC voted that these individuals must undergo skin testing and subsequent VIT, as determined on a case-by-case basis.

Third, the AAC recognized a difference between applicants and designated flight personnel. That is, applicants who have a history of severe anaphylactic reaction to an insect sting or bite must undergo a minimum of 3 years of uncomplicated VIT before being allowed to apply for naval aviation duty. However, designated personnel would be removed from flying activities just long enough to reach a stable maintenance dose of VIT. These individuals would then be allowed to return to aviation duties with no restrictions. The implications of this new policy for applicants are many. Individuals close to the age limit for initial aviation training may find themselves, after 3 years of mandatory VIT, ineligible for naval aviation, having fallen outside the established age limit. In addition, civilian applicants must receive and pay for VIT outside the Navy's system of health care. For active duty applicants who are transferring to an aviation billet and require VIT, the severity of the reaction may influence the Navy's willingness to enter that individual into flight training. If the applicant has experienced too severe a reaction, even with VIT, he or she may have too great a risk to enter into flight training. Also, an individual with a childhood history of sting allergy of any severity who requires VIT may cost the Navy in care and delayed training. This may be grounds for waiver denial. However, in the review of the 182 medical records, any history of sting allergy at any age has been an indication for VIT among aviation candidates thus far. Although this may seem like a great cost to the Navy, the cost is comparable to or even less than that of other therapies and treatments offered without hesitation (Table II). For example, VIT for 5 years is less than one-half the cost of omeprazole treatment for the same period of time.

Finally, the waiver guide also states that those with anaphylactic reactions to an insect sting or bite must receive a challenge dose before being granted a waiver. However, there is no record of any waiver applicant being subjected to a challenge dose. Patients instead have routine repeat skin testing after the completion of VIT. The protective nature of VIT is well established, as is the lessening of the reaction

TABLE II
COMPARATIVE COST OF VIT

	Charge	Tricare Reimbursement
Cost of VIT		
Rush VIT	\$1,280.00	\$798.59
Office visit plus skin test	\$554.00	\$295.88
Maintenance shots (every 6 weeks for 5 years)	\$1,170.00	\$608.15
Total for 5 years of VIT		\$1,739.02 (with \$36.40 Epi-pen)
Comparisons		
Fexofenadine HCl therapy (180 mg/d for 5 years)		\$1,095.00
Omeprazole therapy (20 mg/d for 5 years)		\$3,650.00

The approximate total cost of rush VIT in the Pensacola, Florida, region is shown. The cost is approximately \$1,740 for 5 years of maintenance VIT after 1-day rush VIT. This is less than one-half of the cost for 5 years of once per day omeprazole therapy.

among those who are considered treatment failures. Therefore, skin testing is now the preferred alternative to receiving a challenge dose.

Conclusion

It was clear from our research that the Navy's current aviation waiver policy regarding insect sting allergy did not reflect current clinical guidelines. Our research indicated that the Navy was, in fact, making waiver determinations based not on their published waiver policy but rather on current clinical guidelines. In response to our findings, the Navy's waiver policy was changed using the Navy's official review, voting, and endorsement process. Today the Navy's waiver policy reflects well-founded current clinical guidelines with regard to the need for emergency adrenaline use, unnecessary skin testing and VIT for individuals experiencing mild cutaneous reactions before age 16, and removal of mandatory challenge doses after the completion of VIT. These changes to the Navy's waiver guide pertaining to this subject have been completed and can be viewed online (<http://www.nomi.med.navy.mil>, following the links for the aviation waiver guide).

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