

spirulina's potential allergenicity with both immediate and delayed reactivity. Further studies are needed to better understand this new allergen and its cross-reactivity with other microbial-based foods.

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References

1. Spirulina Ciferri O. The edible microorganism. *Microbiol Rev.* 1983;47(4):551–578.
2. Lupatini AL, Colla LM, Canan C, Colla E. Potential application of microalga *Spirulina platensis* as a protein source. *J Sci Food Agric.* 2017;97(3):724–732.
3. Hosseini SM, Khosravi-Darani K, Mozafari MR. Nutritional and medical applications of *Spirulina* microalgae. *Mini Rev Med Chem.* 2013;13(8):1231–1237.
4. Mueller-Wirth N, Buentner A, Jörg L, Ebo DG, Glatz M, Fernando SL, et al. IgE-mediated chlorhexidine allergy-cross-reactivity with other biguanide disinfectants. *Allergy.* 2020;75(12):3237–3247.
5. Aberer W, Bircher A, Romano A, Blanca M, Campi P, Fernandez J, et al. Drug provocation testing in the diagnosis of drug hypersensitivity reactions: general considerations. *Allergy.* 2003;58(9):854–863.
6. Petrus M, Culerrier R, Campistron M, Barre A, Rougé P. First case report of anaphylaxis to spirulin: identification of phycocyanin as responsible allergen. *Allergy.* 2010;65(7):924–925.
7. Le TM, Knulst AC, Röckmann H. Anaphylaxis to *Spirulina* confirmed by skin prick test with ingredients of *Spirulina* tablets. *Food Chem Toxicol.* 2014;74:309–310.
8. Pimblett P. *Spirulina* allergy; a case history of two patients. *WAO Journal.* 2020;13(8):014.
9. Wilson JM, Platts-Mills TAE. Red meat allergy in children and adults. *Curr Opin Allergy Clin Immunol.* 2019;19(3):229–235.
10. Genitsaris S, Kormas KA, Moustaka-Gouni M. Airborne algae and cyanobacteria: occurrence and related health effects. *Front Biosci (Elite Ed.)* 2011;3(2):772–787.

Vespa velutina nigrithorax venom allergy Real-life clinical practice



Vespa velutina nigrithorax (VVN) is the first hornet accidentally introduced in Europe.¹ In Portugal, the first report was in 2011 in the north (Viana do Castelo).² Bessa et al³ attempted to predict the invasive potential of VVN in the Iberian Peninsula (IP), and through a species distribution model, they concluded that the most suitable areas are in the northern region of the IP. As predicted, most of the nests found in mainland Portugal (12,245 nests in 2018) are situated in northern and central Portugal.⁴

From altering ecosystems to harming economic activities and causing allergic reactions in humans, VVN is making its impact on apiculture, biodiversity, and public health.⁵

At present, there is a scarcity of reports concerning allergic reactions to VVN venom in Portugal. We aim to characterize the reactions and sensitization pattern of patients who have VVN venom allergy in Northern Portugal.

Medical records of patients referred to our department between 2017 and 2020 suspected for having VVN venom allergy were reviewed. *Hymenoptera* venom (HV) allergy diagnostic workup was performed, and results of specific immunoglobulin E (sIgE) to whole extract and molecular components and intradermal skin tests (IDSTs) were evaluated. Sensitization was defined as sIgE levels higher than 0.35 kU/L or a positive IDST result.

A total of 6 patients, 5 men and 1 woman, with ages ranging from 36 to 75 years were included. One was an amateur beekeeper, 2 were road workers, and the remaining did not have any outdoor activities. All were referred because of an allergic reaction after *Hymenoptera* stings. During clinical evaluation, all identified the culprit *Hymenoptera* as VVN and 3 patients claimed that there was a nest nearby the sting location. All episodes occurred outdoors, and half were stung more than once, with a maximum of 3 stings/episode. All patients had anaphylaxis, and symptom onset was within 30 minutes of the sting. All had respiratory symptoms, 4 patients had mucocutaneous, 4 cardiovascular, and 2

gastrointestinal. According to Mueller's modified score, 4 patients had grade III reactions and the remainder had grade IV reactions. After the stings, they underwent medical observation and treatment with corticosteroids and antihistamines. There were 2 patients who were treated with adrenaline.

All had been previously stung by species other than VVN: 2 by wasps, 1 by bees, and 3 by both. None reported systemic reactions; however, half had local large reactions. HV allergy diagnostic workup was performed, and all presented sIgE to *Vespula* spp whole venom, which generally had higher values than sIgE to *Apis mellifera* whole venom. One patient had positive IDST result to *Vespula* spp venom, half to *Polistes* spp venom, and 2 to *A. mellifera* venom. In addition, sIgE levels to *Vespula* and *Polistes* allergic components were evaluated. All tested patients had positive results to Ves v5 and Pol d5, and 4 of 6 were positive to Ves v1. All except 1 patient had higher sIgE values to Ves v5 than Ves v1. He was later stung by wasps with only local large reaction. Baseline tryptase levels were assessed. Only 1 patient had increased values (>8 ng/mL), in whom clonal mast cell disorder was excluded.

The detailed results from the HV allergy diagnostic workup are presented in Table 1.

Vespula spp venom immunotherapy with an ultrarush protocol was started in all patients.

The frequency of stings and thus sensitization to HV allergens depends on geographic, environmental, and ecological factors, which can change over time. VVN introduction in Europe is changing the epidemiology of HV allergy. Chugo et al⁶ first described in Europe a Spanish beekeeper with anaphylaxis after a VVN sting, with sensitization to the vespine antigen 5. Later, 4 components were purified in the venom of European VVN specimens, which are as follows: Vesp v 5, the antigen 5; Vesp v 1, an A1-phospholipase; and 2 hyaluronidases isoforms, Vesp v 2A and 2B. Comparing the phospholipases and antigen 5 of the different genera revealed highest similarity of the VVN components with those of the *Vespa* and *Vespula*, than with *Polistes* species.⁷ Broader populations were approached by Vidal et al.⁸ They

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Table 1
Hymenoptera Venom Allergy Workup

	sIgE (kU/L)		Tryptase (ng/mL)	Intradermal skin tests (μg/mL)						Molecular (kU/L)		
	<i>Apis</i>	<i>Vesp</i>		<i>Vesp</i> 0.1	<i>Vesp</i> 1	<i>Pol</i> 0.1	<i>Pol</i> 1	<i>Apis</i> 0.1	<i>Apis</i> 1	<i>Vesv</i> 1	<i>Vesv</i> 5	<i>Pold</i> 5
P1	0.1	4.2	5.1	NEG	NEG	NEG	NEG	NEG	NEG	0.6	1.8	N/P
P2	N/P	14.3	9.1	NEG	NEG	POS	POS	N/P	POS	2.5	8.1	6.6
P3	6.2	5.7	5.1	D	D	POS	POS	POS	N/P	0.2	3.3	3.2
P4	5.5	15.2	4.3	NEG	POS	POS	POS	N/P	N/P	0.3	3.0	2.8
P5	<0.1	4.8	4.9	N/P	NEG	N/P	NEG	N/P	NEG	3.1	1.9	1.0
P6	N/P	6.9	7.2	NEG	NEG	N/P	NEG	N/P	NEG	1.0	3.9	N/P

Abbreviations: D, dubious; N/P, not performed; NEG, negative; P, patient; Pol, *Polistes* spp; POS, positive; sIgE, specific IgE; Vesp, *Vespula* spp.

found that most patients did not report previous stings by VVN, but from other *Hymenoptera*, especially common wasps. Moreover, the IgE sensitization profile had similarities to that of patients with anaphylaxis to other *vespidae*, and most patients had sIgE to antigen 5 from *Vespula* spp and *Polistes dominula*, which strongly correlated with sIgE to nVesp v 5. They further confirmed nVesp v 5 as a major allergen, and inhibition assay results revealed a better performance of *Vespula* spp venom for inhibiting sIgE binding to VVN, nVesp v 1, and nVesp v 5 than of VVN for *Vespula* spp, rVes v 1, and rVes v 5, suggesting that *Vespula* spp venom was the genuine sensitizer in these cases.⁹

This is the first study regarding hypersensitivity reactions to VVN venom in Portugal. Because specific diagnostic tools for VVN venom allergy are not widely available, *Vespula* spp, *A. mellifera*, and *P. dominula* allergens were used. Our findings support what has been described by Vidal et al⁸ in that all cases presented with anaphylaxis and previous stings by *Hymenoptera* other than VVN. Moreover, a sensitization pattern to *Vespula* spp allergens was found. Surprisingly, IDST results with *Hymenoptera* whole venoms did not translate the sensitization pattern found by the determination of sIgE to the whole venom and molecular components. The development of VVN venom extracts for diagnosis could be advantageous for these patients.

When the venom of the eliciting insect is not accessible for immunotherapy, treatment should be based on patient's sIgE sensitization profile. Taking this in consideration, *Vespula* spp venom immunotherapy was used in our patients. Recently, Rodríguez-Vázquez et al¹⁰ evaluated the usefulness of *Vespula* spp venom immunotherapy in these patients and observed a significant reduction in sIgE and increase in sIgG4 against both VVN and *Vespula* spp venom extract after 12 months of treatment in 46 patients, 28% of which later had field stings by VVN without any systemic reactions. In our population, no patients were restung by VVN; however, all tolerated immunotherapy with *Vespula* spp venom.

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References

- López S, González M, Goldarazena A. *Vespa velutina* Lepeletier, 1836 (Hymenoptera: Vespidae): first records in Iberian Peninsula. *EPPO Bulletin*. 2011;41(3):439–441.
- Grosso-Silva JM, Maia M. *Vespa velutina* Lepeletier, 1836 (Hymenoptera, Vespidae), new species for Portugal. *Arq Entomoloxicos*. 2012;(6):53–54.
- Bessa AS, Carvalho J, Gomes A, Santarém F. Climate and land-use drivers of invasion: predicting the expansion of *Vespa velutina* nigrithorax into the Iberian Peninsula. *Insect Conserv Divers*. 2016;9(1):27–37.
- Instituto Nacional de Investigação Agrária e Veterinária. Bases para a Vigilância Ativa - Plano de Ação para a Vigilância e Controlo da *Vespa velutina*. 2018. Available at: <https://www.inia.pt/plano-acao-vespa-velutina>. Accessed November 29, 2021.
- Monceau K, Bonnard O, Thiéry D. *Vespa velutina*: a new invasive predator of honeybees in Europe. *J Pest Sci*. 2013;87(1):1–16.
- Chugo S, Lizaso MT, Alvarez MJ, Arroabaren E, Lizarza S, Tabar AI. *Vespa velutina* nigrithorax: a new causative agent in anaphylaxis. *J Invest Allergol Clin Immunol*. 2015;25(3):231–232.
- Monsalve R, Gutierrez R, Hoof I, Lombardero M. Purification and molecular characterization of phospholipase, antigen 5 and hyaluronidases from the venom of the Asian hornet (*Vespa velutina*). *PLoS One*. 2020;15(1): e0225672.
- Vidal C, Armisen M, Monsalve R, Gonzalez-Vidal T, Lojo S, Lopez-Freire S, et al. Anaphylaxis to *Vespa velutina* nigrithorax: pattern of sensitization for an emerging problem in Western countries. *J Invest Allergol Clin Immunol*. 2021;31(3):228–235.
- Vidal C, Armisen M, Monsalve R, Gomez-Rial J, Gonzalez-Fernandez T, Carballada F, et al. Vesp v 5 and glycosylated Vesp v 1 are relevant allergens in *Vespa velutina* nigrithorax anaphylaxis. *Clin Exp Allergy*. 2020;50(12):1424–1427.
- Rodríguez-Vázquez V, Armisen M, Gómez-Rial J, Lamas-Vázquez B, Vidal C. Immunotherapy with *Vespa velutina* venom for *Vespa velutina* nigrithorax anaphylaxis: preliminary clinical and immunological results. *Clin Exp Allergy*. 2022;52(2):345–347.

A 2-week medical student curriculum in an outpatient allergy clinic



Outpatient subspecialty rotations have been a fundamental part of the medical student experience, providing initial and sometimes only exposure to several fields, such as Allergy and Immunology. Medical students face several unique challenges in learning during these rotations, including working with multiple preceptors and lack of “down-

time” to discuss topics during a busy clinic day. Providing effective education in the world of Allergy and Immunology clinics presents additional challenges. A 2020 editorial by Pien and Colbert¹ discusses obstacles, such as a lack of allergy specialists who identify teaching as a major clinical interest. Furthermore, the ongoing coronavirus disease 2019 pandemic eliminated many in-clinic experiences for students interested in the field.

Previous studies have attempted to address logistical challenges in medical education with longitudinal curricular interventions,

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