

patient had cyanosis and clubbing. Three United Kingdom cardiovascular centers had confirmed Eisenmenger's syndrome, although he remained active and had an acceptable quality of life. After acute dissection of the pulmonary artery, early death from rupture of the false aneurysm was a certainty.

Closure of the patent ductus arteriosus was necessary because the dissection involved the insertion of the ductus. The intracardiac shunt was

the more important one; we did not close the ventricular septal defect. The patient survived the operation and was discharged from the hospital 10 days later. We therefore disagree with Shuhaiber's suggestion that closure of the patent ductus arteriosus in this patient was "contentious if not dangerous."

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Wine-Induced Anaphylaxis and Sensitization to Hymenoptera Venom

TO THE EDITOR: Alcoholic drinks have been described as triggering or initiating anaphylactoid reactions.¹ Although little is known about the pathogenesis of these reactions,² wine contains many biologic and chemical components derived from grapevines, yeast, bacteria, and insects (including those of the order Hymenoptera) that might explain the observed symptoms.^{3,4}

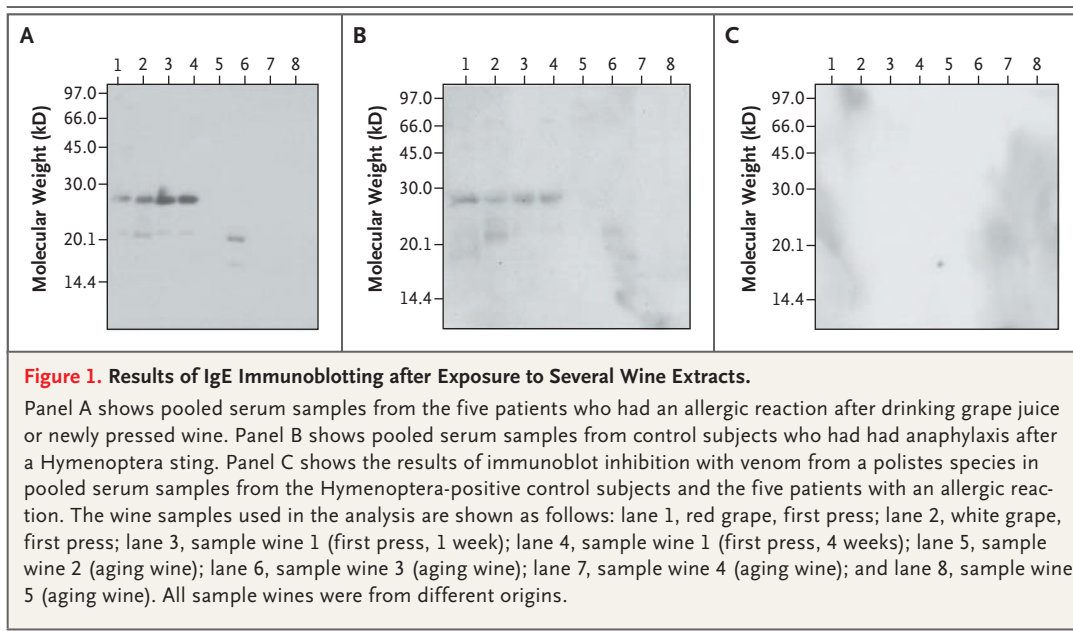
We report on five patients who presented with symptoms after drinking grape juice or newly pressed wines (both red and white). Three of the patients had an oral allergy syndrome and facial flushing, one had asthmatic symptoms, and one had anaphylaxis. Skin tests with conventional allergens, including commercial grape extract, egg white, and wines aged for up to 1 year, were negative. None of the patients had a history of ingesting drugs containing sulfites that was concomitant with these symptoms, nor had any of them been stung by Hymenoptera species. Yet all had positive skin tests for specific IgE antibodies (levels >0.35 kU per liter, CAP, Phadia) to Hymenoptera (*Apis mellifera* and *vespula* and *polistes* species) and to an extract of the wine or grape juice under suspicion for causing the symptoms.

We investigated sensitization to Hymenoptera antigens as a possible cause of these symptoms. The patients with symptoms after drinking red wine were sensitive to both *vespula* and *polistes* species, whereas those with symptoms after drink-

ing white wine were sensitive only to *polistes* species. Patch tests and oral- and bronchial-challenge tests with sulfites were negative in all five patients. Four of the patients had a positive reaction to an oral challenge with the exact wine they had ingested (an oral allergy syndrome and flushing), and in the remaining patient (who had an oral allergy syndrome, flushing, and asthma), there was a 25% fall in the forced expiratory volume in 1 second. Challenges with aging wines were negative. These tests were negative in 6 patients who were not reactive to Hymenoptera antigen and in 12 patients who had had anaphylaxis after a Hymenoptera sting.

Immunoblotting revealed two 22-kD and 27-kD bands for grape juice and freshly pressed wines and one 22-kD band for aging wine in pooled serum samples from the five patients and from the Hymenoptera-positive control subjects. Aging wines (except for sample wine 3) did not show IgE binding to these allergens (Fig. 1). The use of venom extract from *polistes* species as the inhibitory phase (immunoblot inhibition) inhibited these proteins in serum from the patients and from the Hymenoptera-positive control subjects. Immunoblot inhibition with venom extracts from *vespula* species and *A. mellifera* used as the inhibitory phase did not show any inhibition.

Venom antigens found in wines were from venoms of the most prevalent species in Spain.⁴ The development of allergic symptoms after drinking



wine indicates that sensitization to Hymenoptera venom may occur by the oral route.

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Dr. Pineda reports being employed by Diater Laboratories, a pharmaceutical company specializing in the production of allergenic extracts for in vivo diagnosis and treatment of allergies. No other potential conflict of interest relevant to this letter was reported.

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Nephrogenic Systemic Fibrosis, Gadolinium, and Iron Mobilization

TO THE EDITOR: Nephrogenic systemic fibrosis is a newly described systemic disorder that occurs in patients with renal insufficiency.^{1,2} The functional consequences of nephrogenic systemic fibrosis are often devastating and may be fatal. Since nephrogenic systemic fibrosis develops after exposure to gadolinium-containing magnetic resonance contrast agents in some patients,³ the Food and Drug Administration recommended avoiding such agents in patients with renal insufficiency. The mechanism by which nephrogenic

systemic fibrosis develops after gadolinium exposure remains unknown.

Gadolinium is administered as a chelate, since free gadolinium is toxic. Metals such as iron are capable of inducing the dissociation of gadolinium from its chelate (transmetallation). We postulated that some patients with renal insufficiency may have a heightened susceptibility to iron mobilization, which may contribute to gadolinium toxicity and nephrogenic systemic fibrosis. We present prospective data for two patients who had