

# Grape Anaphylaxis: A Study of 11 Adult Onset Cases

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## ABSTRACT

Reports of immunoglobulin E (IgE)-mediated allergic reactions to grapes and wine are limited in the literature. Nevertheless, grapes are widely grown and consumed in Mediterranean countries. The object of this prospective study was to present clinical features, in vivo and in vitro allergy testing, and human leukocyte antigen (HLA) serotyping in patients with recurring reactions to grapes and grape products. Eleven unrelated Greek patients, six men and five women (aged 16–44 years; mean, 26.9 years) were enrolled based on a documented history of IgE-mediated reactions to grapes, wine, or other grape products. Their evaluation included full history, reaction severity, clinical examination, skin-prick tests with food allergens and molds, serum IgE, specific IgEs to the same allergen battery, and HLA typing. Patients reported 35 grape-induced anaphylaxis episodes ranging from moderate (more than one system involved but not prominent respiratory or cardiovascular symptoms; 45.5%) to severe (serious respiratory obstruction and/or hypotension and loss of consciousness; 54.5%). A causative agent was identified: wine, 10/35 (28.6%); red grapes, 9/35 (25.7%); stuffed vine leaves, 8/35 (22.9%); raisins, 3/35 (8.6%); white grapes, 2/35 (5.7%); wine vinegar, 2/35 (5.7%); and grape juice, 1/35 (2.9%). Other foods that induced anaphylaxis were apples (54.5%), cherries (18.6%), peaches (18.6%), and bananas (9.3%). Specific IgE values were in accordance with skin-prick tests reactivity. Concerning HLA typing, 9/11 possessed HLA-DR11(5) and -DQ7(3) and the remaining two possessed

HLA-DR17(3) and -DQ2 antigens. Grapes, wine and other grape products might cause serious allergic reactions in sensitized individuals. The cosensitization and reaction incidence to other fruit allergens could be a basis for further investigation of panallergens of fruits. HLA class II antigens may contribute in genetic predisposition to these allergic reactions. (Allergy and Asthma Proc 26:53–58, 2005)

Food-induced anaphylaxis has become the leading cause of anaphylactic reactions that occur outside of hospitals; the vast majority of food-induced allergic reactions are caused by a limited number of foods.<sup>1</sup> Fruits belong to several botanical families but only a small number have been proven objectively to cause immunoglobulin E (IgE)-mediated allergic reactions.

Grapes are widely grown in the Mediterranean area as well as in other temperate and subtropical regions. The only species cultivated in our country and in other main grape-producing countries such as Italy and Spain is *Vitis vinifera*, which belongs to the subfamily Ampelidae of the Vitaceae family. Grapes are widely consumed in Greece as fresh fruit, juice, and wine, and the boiled vine leaves are used for the preparation of stuffed vine leaves, the so-called “dolmades.” The recent changes in dietary habits and the global market make possible the consumption of grapes or its products in almost any place in the world; this fact probably implies extended exposure and increased reaction rate.

Allergic reactions to grapes and wine are reported rarely in medical literature and as far as wine is concerned, they are commonly attributed to sulfites.<sup>2</sup> Most of the reactions are described as case reports and refer to oral allergy syndrome (OAS),<sup>3,4</sup> systemic reactions in two patients previously presenting OAS,<sup>5</sup> multiple severe anaphylactic episodes,<sup>6</sup> exercise-induced anaphylaxis,<sup>7,8</sup> and anaphylactic reactions due to American grape sensitization (*Vitis labrusca*).<sup>9</sup>

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In this study, we present 11 patients with several adult-onset anaphylactic reactions to grapes or grape products. Besides the clinical findings and the allergy investigation of the cases presented here, human leukocyte antigen (HLA) typing was performed to detect possible correlation of grape IgE-mediated hypersensitivity with specific HLA genotypes.

## METHODS

### Patients

The study included 11 unrelated patients of Greek origin who presented for medical advice, to the Allergy Department of the Andreas Sygros Hospital of the University of Athens, with a history of allergic reaction after consumption of grapes (red/white) or grape products (red wine, white wine, juice, wine vinegar, and stuffed vine leaves) from March 2001 to April 2003. The Andreas Sygros Hospital Scientific Committee approved the study plan before patient recruitment.

A detailed clinical history emphasizing the species of the grape or its grape products, the time interval until the onset of symptoms, the full clinical presentation, and the management of the reaction was obtained from every patient. Personal or familial atopic status and previous allergic reactions due to other causative agents were recorded. Detailed clinical examination of every patient took place to exclude other misleading underlying diseases. Moreover, single-blind placebo-controlled oral challenges with potassium metabisulfite (capsules containing 5–50 mg) were performed to ensure the absence of intolerance to sulfites among our population.

Allergic sensitization to grapes was confirmed by (i) skin-prick tests (SPTs), using a commercial kit and the fresh fruits (red and white species) and (ii) measurement of serum grape-specific IgE. The same procedure was used for the investigation of cosensitization to other food allergens including peanuts and tree nuts (hazelnuts, almonds, pistachios, and walnuts), fresh fruits (cherries, oranges, strawberries, apples, bananas, and peaches), legumes (beans, soybeans, chickpeas, fresh peas, and lentils), and molds (*Cladosporium*, *Aspergillus*, and *Alternaria*), which can be present on the fruit surface. Patients sensitive to food allergens consumed simultaneously with grapes before the reported reactions were excluded from this study.

The reported reactions were classified according to their severity in a four-point scale as follows: 1 = generalized urticaria, itching, malaise, and/or anxiety; 2 = any of the reactions in point 1, plus two or more of the following: angioedema, constriction in chest, nausea, vomiting, diarrhea, abdominal pain, and/or dizziness; 3 = any of the reactions in points 1 and 2, plus two or more of the following: dyspnea, wheezing, stridor (any of these alone are grade 3), dysphagia, dysarthria, hoarseness, weakness, confusion, and/or feeling of impending disaster; 4 = any of the reactions in points 1–3, plus two or more of the following:

fail in blood pressure, collapse, loss of consciousness, incontinence, and/or cyanosis. Blood samples were drawn from each patient for HLA typing and serum was stored at  $-80^{\circ}\text{C}$  until use in *in vitro* tests.

### Skin Testing

SPTs were performed using standard techniques to the battery of allergens mentioned previously (Dome-Hollister, France, and ALK, Denmark). Positive (histamine phosphate solution, 2.7 mg/mL, equivalent to 1 mg/mL of histamine base) and negative controls were used also. Moreover, because of the presence of labile antigens in fresh fruit extracts and the frequent failure to obtain positive skin reactions in clinically sensitive patients, we performed SPTs using the prick-to-prick technique according to the method of Dreborg and Foucard.<sup>10</sup> To obtain a permanent record, the size of the reaction was outlined with a ballpoint pen after 20 minutes, transferred onto cellophane tape, and stored on paper. The wheal and erythema size were taken into consideration to assess the positivity; wheal diameter  $>3$  mm and erythema  $>10$  mm were regarded as positive. The positive reactions were classified in a four-point scale as follows: 1+ = 3- to 4-mm wheal diameter, 2+ = 5- to 8-mm wheal diameter, 3+ =  $>8$ -mm wheal diameter without pseudopodia, and 4+ = any wheal diameter with pseudopodia or satellite wheals.

### In Vitro Diagnostic Methods

IgE concentration in serum was measured using a fluorometric enzyme immunoassay and the results were expressed in international units per milliliter. Allergen-specific IgE antibodies were detected with a commercial microplate assay kit (Real Test, Lopharma, Italy) and were classified in a five-point scale: 1+ =  $<0.35$  kU/L, 2+ = 0.35–0.70 kU/L, 3+ = 3.5–17.5 kU/L, 4+ = 17.5–32.0 kU/L, and 5+ =  $>32$  kU/L.

### HLA Typing

Patients' and controls' (110 healthy Greek individuals) HLA-typings were performed by serological and molecular (polymerase chain reaction–sequence-specific primers) techniques.<sup>11–13</sup> All known HLA-A, -B, -C, -DR, and -DQ antigens were determined.

### Statistical Analysis

Correlations were performed using the Kendall rank correlation coefficient ( $\tau$ ) because it is considered the preferable statistical test for ordinal variables with small sample sizes. Statistical significance was assumed at  $p < 0.05$ , and data are expressed as means  $\pm$  SD.

## RESULTS

### Patients

Eleven patients, 6 men and 5 women (mean age, 26.9 years; range, 16–44 years) were enrolled in this study based on a documented history of IgE-mediated allergic reactions to grapes, wine, or other grape products. The first reaction was presented almost 4 years earlier (mean age, 23.1 years; range, 13–38 years).

Of the 11 patients, only 3 (27.3%) patients reported a family history of atopy while 5/11 (45.5%) patients had symptoms of atopic diseases. The patients' main allergy data and the clinical manifestations of the anaphylaxis episodes are shown in Table I. Every patient reported exactly the same symptoms in every reaction without increasing severity, irrespective of the time interval between the episodes. The severity of the anaphylaxis episodes ranged from moderate, referring to class 2 according to the previously described four-point scale classification (5/11 patients, 45.5%), to severe, classes 3 and 4 at the same system (6/11 patients, 54.5%). The onset of symptoms varied from 1 to 140 minutes after grape consumption (mean = 67.2 minutes; SD = 12.2). The duration of each reported reaction was determined from 17 to 240 minutes (mean = 98.7 minutes; SD = 29.2) but in most cases (32/35 documented episodes) the clinical course was modified by treatment because 9/32 used their one emergency kit (antihistamines, self-injected adrenaline, corticosteroids, and inhaled  $\beta_2$ -agonists) according to their symptoms while 23/32 reactions were treated at the Emergency Department.

Table II presents the number of reported reactions and the exact causative grape product as well as the reactions to other food allergens. Furthermore, 8/11 patients reported symptoms of OAS after grape consumption before the onset of systemic reactions. Clinical manifestations of anaphylaxis were reported after consumption of the following kinds of food: 10/35 (28.6%) patients, after drinking wine (five red and four white wines and one sparkling wine); 9/35 (25.7%) patients, after red grape consumption; 8/35 (22.9%) patients, after ingestion of stuffed vine leaves; 3/35 (8.6%) patients, after raisin consumption; 2/35 (5.7%) patients, due to white grapes; 2/35 (5.7%) patients, after eating salads with wine vinegar; and 1/35 (2.9%) patients, after drinking grape juice. The prevalent causative agents of food, other than grapes, inducing anaphylaxis in these patients were apples (6/11; 54.5%), cherries (2/11, 18.6%), peaches (2/11, 18.6%), and bananas (1/11; 9.3%).

### SPTs

Skin reactivity to grapes was found identical with both techniques used in 10/11 patients with only slight differences in the one left. According to the classification described previously, reactions ranged from classes 3+ to 4+ (mean = 3.9; SD = 0.3). The positive skin tests of each patient are depicted in Table I. Skin reactivity to molds was

not found; the positive SPTs could not be attributed to the presence of fungi on the grape surface.

According to the grading system of the SPTs used, the most profound skin reactivity, referring to the prick-to-prick technique, to other fruits was found in apples (mean = 3.45; SD = 0.83), peaches (mean = 3.27; SD = 1.2), cherries (mean = 3.18; SD = 0.75), strawberries (mean = 2.19; SD = 1.78), peanuts (mean = 2.73; SD = 1.43), and walnuts (mean = 2.37; SD = 1.69).

### In Vitro Diagnostic Methods

IgE serum levels had a great variability and ranged from 4.0 to 1457.0 IU/mL (mean = 359.1; SD = 345.5). Grape-specific IgE was elevated and expressed in either kilounit per liter (mean = 14.11 kU/L; SD = 12.82; range, 4.01–48.70) or classes (mean = 3.27; SD = 0.90; range, 2–5).

Among the other allergens tested, strong positivity was found in apples (mean class = 2.72; SD = 0.90), peaches (mean class = 2.55; SD = 1.21), and cherries (mean class = 2.45; SD = 0.52).

### HLA Typing

HLA antigen typing in our patients is presented in Table III. HLA-DR11<sup>5</sup> was found in 9 of 11 patients (81.8% versus 50% in controls). The two remaining patients possessed HLA-DR17<sup>3</sup> (18.2% versus 17.6% in controls).

### Correlations

Statistical analysis did not establish correlations between clinical features of the reported reactions (time of symptom onset after grape consumption, severity, and/or number of previous grape anaphylaxis episodes) and *in vivo* or *in vitro* diagnostic procedures (SPT positivity, Real Test class, and serum IgE).

A similar pattern was observed in skin reactivity and grape-specific IgE, although it did not reach statistical significance. Contrarily, prick-to-prick positivity and Real Test class in apples and cherries were significantly related ( $p = 0.019$  and  $p = 0.01$ , respectively).

## DISCUSSION

In this study, we described 11 adult patients with reported allergic reactions to fresh grapes (red or white *Vitis vinifera* species), wine, stuffed vine leaves, grape juice, raisins, and wine vinegar. All but one had repeated reactions, especially in wine and stuffed vine leaves, probably because they did not initially recognize their relationship with the fresh fruit.

The description of 11 cases is, to our knowledge, the second in size after a recent Italian study including 14 patients.<sup>14</sup> The IgE-mediated type of reactions was shown clearly by *in vivo* and *in vitro* testing while the clinical presentation of each episode confirmed anaphylaxis. Moreover, before the reported reactions, patients did not take any

TABLE I

| Patient's Allergic Data and Clinical Presentation for Grape Allergy |          |     |                                                                                                               |                     |                            |                                                                              |
|---------------------------------------------------------------------|----------|-----|---------------------------------------------------------------------------------------------------------------|---------------------|----------------------------|------------------------------------------------------------------------------|
| Patient No.                                                         | Age (yr) | Sex | Symptoms (Grape/Wine/Grape Products)                                                                          | Prick-to-Prick Test | Real Test (Lopharma; kU/L) | Positive Skin Tests to Other Foods and Fungi                                 |
| 1                                                                   | 20       | M   | Urticaria/AO, sneezing, cough, dyspnea, hoarseness, vomiting, diarrhea, abdominal pain                        | 4+                  | 9.21                       | Peanut, tree nuts, cherry, strawberry, apple, peach                          |
| 2                                                                   | 16       | F   | Urticaria/AO, cough, vomiting, diarrhea                                                                       | 4+                  | 9.88                       | Peanut, cherry, apple                                                        |
| 3                                                                   | 26       | F   | Urticaria/AO, sneezing, cough, dyspnea, constriction in chest, diarrhea, abdominal pain                       | 4+                  | 6.76                       | Peanut, tree nuts, cherry, strawberry, apple, banana, peach, legumes         |
| 4                                                                   | 18       | M   | Urticaria/AO, sneezing, cough, dyspnea, constriction in chest, hoarseness, vomiting, diarrhea                 | 4+                  | 15.93                      | Peanut, tree nuts, cherry, strawberry, apple, banana, peach, orange, legumes |
| 5                                                                   | 27       | F   | Urticaria/AO, sneezing, cough, vomiting, abdominal pain                                                       | 4+                  | 4.01                       | Peanut, tree nuts, cherry, strawberry, apple, banana, peach                  |
| 6                                                                   | 40       | F   | Urticaria/AO, sneezing, cough, dyspnea, constriction in chest, diarrhea, abdominal pain                       | 4+                  | 7.77                       | Peanut, tree nuts, cherry, apple, banana, peach                              |
| 7                                                                   | 44       | M   | Urticaria/AO, sneezing, cough, vomiting, diarrhea, abdominal pain                                             | 3+                  | 8.80                       | Tree nuts, cherry, apple, peach                                              |
| 8                                                                   | 24       | M   | Urticaria/AO, vomiting, diarrhea                                                                              | 4+                  | 5.53                       | Peanut, tree nuts, cherry, strawberry, apple, peach, legumes                 |
| 9                                                                   | 31       | F   | Urticaria/AO, sneezing, cough, dyspnea, hoarseness, constriction in chest, vomiting, diarrhea, abdominal pain | 4+                  | 24.27                      | Cherry, strawberry, apple, peach                                             |
| 10                                                                  | 28       | M   | Urticaria/AO, cough                                                                                           | 4+                  | 48.7                       | Peanut, tree nuts, cherry, apple, strawberry, peach                          |
| 11                                                                  | 22       | F   | Urticaria/AO, sneezing, cough, hoarseness, diarrhea                                                           | 4+                  | 14.37                      | Peanut, walnut, cherry, apple, peach                                         |

*M = male; F = female; AO = angioedema.*

*M* = male; *F* = female; *AO* = *angioedema*.

TABLE II

## Causative Agents of Anaphylaxis Episodes in our Patients

| Patient No. | No. of Episodes (Grape/Wine/ Grape Products) | Causative Agent                                     | No. of Episodes (Other) | Causative Agent | Reaction Severity |
|-------------|----------------------------------------------|-----------------------------------------------------|-------------------------|-----------------|-------------------|
| 1           | 3                                            | Red grape, red wine, white wine                     | 0                       | —               | 3                 |
| 2           | 2                                            | White grape, wine vinegar                           | 1                       | Apple           | 2                 |
| 3           | 3                                            | Red grape, white wine, grape plant leaves           | 2                       | Cherry, peach   | 3                 |
| 4           | 1                                            | Red grape                                           | 2                       | Apple, banana   | 3                 |
| 5           | 5                                            | Red wine (2), grape plant leaves (2), white wine    | 0                       | —               | 2                 |
| 6           | 4                                            | Red grape, white grape, red wine, sparkling wine    | 1                       | Apple           | 3                 |
| 7           | 3                                            | Red grape, grape plant leaves (2)                   | 2                       | Cherry, Peach   | 2                 |
| 8           | 2                                            | Red grape, white wine                               | 1                       | Apple           | 2                 |
| 9           | 4                                            | Red grape, raisin, grape plant leaves, wine vinegar | 1                       | Apple           | 3                 |
| 10          | 5                                            | Red grape, red wine, raisin, grape plant leaves (2) | 0                       | —               | 2                 |
| 11          | 3                                            | Red grape, raisin, grape juice                      | 1                       | Apple           | 3                 |

TABLE III

## HLA Typing of Patients

| Patient No. | HLA Region         |                     |             |             |                     |                   |               |
|-------------|--------------------|---------------------|-------------|-------------|---------------------|-------------------|---------------|
|             | A                  | B                   | Bw          | Cw          | DR                  | DQ                | DRw           |
| 1           | A1,<br>A26(10)     | B51(5),<br>B61(40)  | —           | —           | DR11(5),<br>DR14(6) | DQ5(1)<br>DQ7(3)  | DR52          |
| 2           | A23(9),<br>A33(19) | B49(21),<br>B58(17) | Bw4         | Cw3         | DR16(2),<br>DR17(3) | DQ5(1)<br>DQ2     | DR51,<br>DR52 |
| 3           | A2,<br>A66(10)     | B18,<br>B41         | Bw6         |             | DR11(5),<br>DR13(6) | DQ7(3)            | DR52          |
| 4           | A2,<br>A32(19)     | B51(5),<br>B35      | Bw4,<br>Bw6 | Cw4         | DR11(5),<br>DR10    | DQ5(1)<br>DQ7(3)  | DR52          |
| 5           | A2                 | B51(5),<br>B60(40)  | Bw4,<br>Bw6 | Cw3,<br>Cw5 | DR11(5),<br>DR14(6) | DQ5(1)<br>DQ7(3)  | DR52          |
| 6           | A1,<br>A3          | B49(21),<br>B62(15) | —           | Cw3         | DR11(5)             | DQ7(3)            | DR52          |
| 7           | A24(9)             | B49(21),<br>B62(15) | Bw4,<br>Bw6 | Cw7         | DR4,<br>DR11(5)     | DQ7(3),<br>DQ8(3) | DR52,<br>DR53 |
| 8           | A24(9),<br>A32(19) | B38(16),<br>B35     | Bw4,<br>Bw6 | Cw4         | DR4,<br>DR11(5)     | DQ7(3)            | DR52,<br>DR53 |
| 9           | A1,<br>A66(10)     | B52(5),<br>B18      | Bw4,<br>Bw6 | Cw7         | DR11(5),<br>DR15(2) | DQ6(1),<br>DQ7(3) | DR51,<br>DR52 |
| 10          | A2,<br>A24(9)      | B39(16),<br>B35     | Bw6         | Cw4         | DR11(5),<br>DR16(2) | DQ5(1)<br>DQ7(3)  | DR51,<br>DR52 |
| 11          | A24(9),<br>A32(19) | B8,<br>B35          | Bw6         | Cw4,<br>Cw7 | DR17(3)             | DQ2               | DR52          |

medication and had not consumed other foods to which they were sensitized. However, high concentrations of sulfites can be found in wine, dried fruits (raisins), and juices but after ingestion of these agents, reactors experience mainly flushing, bronchospasm, and hypotension<sup>15</sup>; the reactions described in this study were much different than typical urticaria and angioedema as main clinical manifestations.

In the population of our study, all 35 documented reactions to grapes appeared to be moderate to severe and each

patient reproduced the same symptoms in repeated episodes. In the literature, severe and even near fatal anaphylaxis episodes have been reported. A 28-year-old woman presented with generalized urticaria/angioedema, dyspnea, and hypotension after eating a bunch of white grapes.<sup>6</sup> Two French patients with known OAS to grapes developed anaphylactic shock and severe exercise-induced anaphylaxis, respectively, in reexposure.<sup>5</sup> In accordance with our findings, a 44-year-old man with several anaphylactic reactions

from selective sensitization to Americana grapes reproduced the same moderate to severe clinical presentation in each episode.<sup>8</sup> We also think that a point of interest is the varying time between grape consumption (1–140 minutes) and onset of symptoms; similar data are hard to find in published studies on grape allergy.

The most impressive clinical finding in this study seems to be the prevalence of cosensitization and the documented anaphylactic reactions to certain fruits: 11/11 and 6/11, respectively, in apples; 10/11 and 2/11 in peaches; and 11/11 and 2/11 in cherries. In the recent Italian study mentioned previously,<sup>13</sup> the prevalent cosensitizations among grape-allergic patients were 9/14 to peaches, 5/14 to cherries, and 5/14 to apples. In this very interesting study, researchers have characterized the most important allergens of grape as endochitinases 4A and B, a lipid transfer protein, and a thaumatin-like protein while only endochitinase 4A is responsible for allergic reactions to wine. Grapes are botanically far from the Rosaceae family in which apples (Pomoideae subfamily), peaches, and cherries (Prunoideae subfamily both) belong. Nevertheless, lipid transfer proteins, which are relevant to apple and peach allergens, considering their ubiquitous distribution in tissues of many plant species, could be a novel type of panallergen of fruits and vegetables.<sup>16</sup>

Several studies have suggested that allergen recognition and antibody responses are influenced genetically by HLA or HLA-linked genes. These studies were based on the knowledge that the HLA class II antigens DR and DQ are involved directly in the presentation of peptide fragments of allergens to CD4<sup>+</sup> T cells.<sup>17</sup> Susceptibility to allergies to several trees, grasses, weeds, dust mites, and peanuts has been associated with different HLA class II DR antigens.<sup>18,19</sup> It is interesting to note that 9 of the 11 patients possess HLA-DR11<sup>5</sup> antigen and the 2 remaining patients have HLA-DR17<sup>3</sup> antigen. The frequency of these two HLA antigens in the Greek population is 50 and 17.6%, respectively. Clearly, additional studies are needed to clarify the role of HLA class II associations with sensitization and clinical futures in specific allergens.

In conclusion, we described several cases of repeated IgE-mediated reactions to grapes, wine, and other grape products. Similar clinical manifestations in different courses of grape allergen, almost identical prevalent cosensitizations to other already known allergenic fruits, and the first determination of HLA antigens in grape-allergic patients are the core of this study. We suggest that allergy to grapes may not be as uncommon as generally believed in the literature

and should be considered as a possible offending cause in certain episodes of food-induced anaphylaxis probably in genetically at-risk individuals.

## REFERENCES

1. Sampson HA. Food allergy. Immunopathogenesis and clinical disorders. *J Allergy Clin Immunol* 103:717–728, 1999.
2. Settupane GA. The restaurant syndromes. *Arch Intern Med* 146: 2129–2130, 1986.
3. Giannoccaro F, Munno G, Riva G, et al. Oral allergy syndrome to grapes. *Allergy* 53:451–452, 1998.
4. Rodriguez A, Trujillo MJ, Matheu V, et al. Allergy to grape: A case report. *Pediatr Allergy Immunol* 12:289–290, 2001.
5. Guinnee MT, Rassemont R, and Laurent J. Le raisin est aussi un trophallergene. *Rev Fr Allergol* 37:400, 1997.
6. Vaswani SK, Chang BW, Carey RN, et al. Adult onset grape hypersensitivity causing life threatening anaphylaxis. *Ann Allergy Asthma Immunol* 83:25–26, 1999.
7. Senna G, Mistrello G, Roncarolo D, et al. Exercise-induced anaphylaxis to grape. *Allergy* 56:1235–1238, 2001.
8. Dohi M, Suko M, Sugiyama H, et al. Food dependent, exercise-induced anaphylaxis: A study of eleven Japanese cases. *J Allergy Clin Immunol* 87:34–40, 1999.
9. Bircher AJ, Bigliardi P, and Yilmaz B. Anaphylaxis resulting from selective sensitization to Americana grapes. *J Allergy Clin Immunol* 104:1111–1113, 1999.
10. Dreborg S, and Foucard T. Allergy to apple, carrot, and potato in children with birch pollen allergy. *Allergy* 38:167–172, 1983.
11. Terasaki PI, and McClelland JD. Microdroplet assay of human serum cytotoxins. *Nature* 204:998–1000, 1964.
12. Vartral F, Gaudernack G, Funderud S, et al. HLA class I and II typing using cells positively selected from blood by immunomagnetic isolation—a fast and reliable technique. *Tissue Antigens* 28:301–312, 1986.
13. Olerup O, and Zetterquist H. HLA-DR typing by PCR amplification with sequence-specific primers (PCR-SSP) in 2 hours: An alternative to serological DR typing in clinical practice including donor-recipient matching in cadaveric transplantations. *Tissue Antigens* 39:225–235, 1992.
14. Pastorello EA, Farioli L, Pravettoni V, et al. Identification of grape and wine allergens as an endochitinase 4, a lipid transfer protein and a thaumatin. *J Allergy Clin Immunol* 111:350–359, 2003.
15. Simon RA. Adverse reactions to food and drug additives. *Immunol Allergy Clin North Am* 16:137–176, 1996.
16. Sanchez-Morge R, Lombardero M, Garcia-Selles FJ, et al. Lipid-transfer proteins are relevant allergens in fruit allergy. *J Allergy Clin Immunol* 103:514–519, 1999.
17. Huang SK, and Marsh DG. Genetics of allergy. *Ann Allergy* 70:347–359, 1993.
18. Sandford AJ, Weir TD, and Pare PD. Phenotypic heterogeneity in asthma and allergy. *Clin Exp Allergy* 28:26–31, 1998.
19. Howell WM, Turner SJ, O'B Houricane J, et al. HLA class II DRB1, DQB1, and DPB1 genotypic associations with peanut allergy: Evidence from a family based and case-control study. *Clin Exp Allergy* 28:156–162, 1998. □

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