auto-injector (κ = 0.57, 95% CI 0.38-0.76), and less agreement between self-reported peanut allergy and peanut allergy defined by the 90% specificity decision point only (κ = 0.49, 95% CI 0.31-0.68).

Each epidemiologic method for assessing peanut allergy prevalence has strengths and limitations. Double-blind, placebo-controlled food challenges are the gold standard for clinical peanut allergy diagnosis, but these are challenging to implement in large, unselected cohorts and have not been done in unselected US cohorts.[2] As diagnostic adjuncts, component resolved diagnostics may also be increasingly implemented in epidemiologic cohorts going forward. In this letter, we have provided prevalence estimates according to several criteria that can be compared to one another and to previous estimates. Our results come from a US cohort of children not selected for allergy or any disease, and they support that peanut allergy is an increasingly prevalent condition.

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This study was supported by the National Institutes of Health (NIH AI093538, HL61907, HL64925, HD34568, AI35786, HL68041, and AI102960).

Disclosure of potential conflicts of interest: S. Bunyavanich and T. A. E. Platts-Mills have received research support from the National Institutes of Health/National Institute of Allergy and Infectious Diseases. L. Workman and D. R. Gold have received research support from the National Institutes of Health. J. E. Sordillo has received research support from the National Heart, Lung, and Blood Institute. M. W. Gillman has received royalties from UpToDate and Cambridge University Press. A. A. Litonjua has received research support from the National Institutes of Health and has received royalties from UpToDate and Springer Humana Press. The rest of the authors declare that they have no relevant conflicts of interest.

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Available online July 30, 2014.
http://dx.doi.org/10.1016/j.jaci.2014.05.050

Galactose-alpha-1,3-galactose sensitization is a prerequisite for pork-kidney allergy and cofactor-related mammalian meat anaphylaxis

To the Editor:

Delayed type I reactions to red meat are typical for patients sensitized to galactose-alpha-1,3-galactose (α-Gal), and increasing numbers of patients are being recognized worldwide.[1,2] Interestingly, allergic reactions to pork kidney are mainly observed in Europe and are a good example of how regional differences in meat consumption can influence the clinical presentation of this specific variant of type I allergy.[3] The aim of this study was to outline how an understanding of allergy to pork kidney can be helpful for the understanding of red meat allergy in general.

Based on clinical history, 25 German patients (9 female, 16 male; median age 56 years; Table I) with a history of at least 1 allergic reaction to pork kidney were selected and analyzed. The consumption of pork kidney led to anaphylaxis in 72% of the patients (according to the Ring and Messmer severity scale,[4] 56% of those were grade II, and 44% were grade III) and to urticaria/angioedema without extracutaneous manifestations in the remaining 28%. Using structured interviews, cofactors of anaphylaxis[5] could be identified in 81% of the patients (21/25 patients, Table I). Additional systemic allergic reactions to other mammalian meat, dairy products, or gelatin were reported in 56% of the patients (Table I). Based on the reported time between consumption of pork kidney and onset of the first symptoms, the reactions were classified as immediate type I reactions (≤3 hours) and delayed type I reactions (3 to 6 hours). In this cohort (n = 21; mean reaction time 1.25 hours; range 0.25 to 8.0 hours), 67% were immediate type I reactions. Interestingly, patients with a history of hypersensitivity to pork kidney only (n = 9; mean reaction time 3.5 hours; range 0.5 to 8.0 hours) were evenly distributed between the immediate type I reaction and the delayed type I reaction groups (ratio 1.25:1). In contrast, patients with hypersensitivity to both pork kidney and red meat (n = 11) reacted earlier, with an immediate type I reactions/delayed type I reactions ratio of 3:1 (mean reaction time 1.5 hours; range 0.25 to 5.0 hours). Two or more associated cofactors (ratio 3.5:1) and anaphylaxis (grades II and III) were linked to immediate type I reactions (ratio 2:1).

Commercially available skin prick tests from pork, beef, lamb, or horse meat extracts elicited reactions in only 2 patients, milk extracts in 0 patients. In contrast, prick-to-prick tests using raw and cooked pork kidney showed 100% sensitivity, higher than raw and cooked beef kidney and muscle meat of different species (Fig 1). The process of cooking beef and pork meat decreased sensitivity in prick-to-prick tests. The pattern of prick-to-prick test results was comparable in patients with only pork-kidney

TABLE I. Clinical characteristics of 25 α-Gal–sensitized patients allergic to pork kidney

					Pork kidney			Mammalian meat		Oral	sIgE
Patient (no.)	Age (y)	Sex	Duration of allergy	Events (no.)	Symptoms	Delay (min)	Cofactors (code)	Muscular meat	Other	Challenge	α-GAL (kUa/L)
1	56	M	39 y	3	Urt	480	1	No		Yes	3.12
2	69	M	1.5 y	3	Ana III	270	4	No	Lung, heart	Yes	2.87
3	47	M	10 y	>10	Ana II	45	n/a	Pork, beef, deer	Sausages, gelatin	Yes	69.30
4	32	M	6 mo	2	Ana II	90	0	No		Yes	15.50
5	66	M	2.8 y	5	Urt	30	3, 4	Pork	Sausages	Yes	60.10
6	56	F	10 y	2	Urt	n/a	n/a	Pork		Yes	65.90
7	52	F	1.1 y	2	Ana II	30	0	No		No	1.22
8	77	M	3 mo	1	Ana III	30	1, 2, 4	No		No	41.00
9	55	M	12 y	5	Ana III	240	n/a	Pork, beef		Yes	9.13
10	41	F	3 mo	3	Ana III	15	0	No	Sausages, milk	No	84.10
11	73	F	2.4 y	2	Ana II	240	2	Pork, beef		No	11.90
12	53	M	28 y	1	Urt	n/a	n/a	No		No	1.56
13	56	M	19 y	3	Ana II	45	n/a	Pork, deer		No	45.60
14	54	F	24 y	3	Ana III	120	2	Lamb	Sausages	No	9.18
15	62	F	25 y	>10	Ana II	45	n/a	Pork, beef, Lamb		No	2.10
16	72	M	2.2 y	2	Ana II	90	1, 2, 3	Pork		No	11.80
17	76	M	1 mo	1	Ana II	300	1	No		No	48.50
18	68	F	8 mo	7	Ana III	30	2,4	Pork, beef	Sausages, tripe	No	18.90
19	55	F	6 y	1	Urt	120	0	No		Yes	15.40
20	52	M	1 mo	1	Ana II	60	1	No		No	9.30
21	65	F	21 y	>10	Ana II	30	2	Pork, beef		No	63.30
22	70	M	1 mo	1	Ana III	300	3	No		No	18.40
23	55	M	16 y	2	Ana II	180	2	No	Sausages	No	13.20
24	61	M	20 y	3	Urt	n/a	n/a	Beef		No	67.60
25	72	M	52 y	3	Urt	n/a	n/a	No		No	3.50

Cofactors: 0 = none, 1 = exercise, 2 = alcohol, 3 = nonsteroidal anti-inflammatory drug, 4 = ACE inhibitor/β-agonist.
Ana, Anaphylaxis (according to Ring and Messmer); *F*, female; *M*, male; *n/a*, not available; *Urt*, urticaria.

allergy and patients with additional red meat allergy in their clinical history. Intradermal testing with gelatin-derived colloid (Gelafundin 4%, B. Braun, Melsungen, Germany) proved to be a test alternative to prick-to-prick tests with fresh meat (sensitivity 85%).[6] Prick-to-prick tests with fresh meat (n = 5) and intradermal testing with gelatin-derived colloid (n = 10) performed for other medical reasons in α-Gal–negative individuals were always negative and serve as controls for this study. Cat dander, containing possible cross-reacting allergens, was reactive in 38% of the prick tests. Based on history, cosensitization and total IgE 60% of the patients were classified as atopics. Serum IgE to α-Gal was detected in all patients using an experimental ImmunoCAP produced by Phadia AB (Uppsala, Sweden) with covalent coupling of natural purified bovine thyroglobulin to ImmunoCAP solid phase (Table I and Table E1, in this article's Online Repository at www.jacionline.org). Additionally, specific IgE was analyzed to the following (% of reactive samples): pork (92%) and beef meat (96%), pork serum albumin (0%) and beef serum albumin (14%), cat dander (44%) and milk (43%; Table E1). *In vitro* assays with serum from 2 selected patients were performed to investigate whether reactivity to pork kidney is mediated by IgE to α-Gal and whether reactivity to pork muscle meat is mainly dependent on IgE to α-Gal. Importantly, IgE reactivity with α-Gal could be completely blocked by pre-incubating the serum with pork-kidney extracts, proving IgE cross-reactivity (Fig 2). Moreover, reactivity to pork meat using the ImmunoCAP assay was also completely blocked by pre-incubation with both pork-kidney extract and bovine thyroglobulin, demonstrating that in these patients, IgE recognition of the meat extract depends on IgE to α-Gal.

To verify the diagnosis and to assess the individual risk of developing anaphylaxis, including possible cofactors, a total of 35 oral challenge tests (OCT) in 4 patients with exclusive pork-kidney allergy and 4 patients with additional red meat allergy were performed (Table II). OCT with pork kidney was reactive in all patients except for 1 patient, who only had pork-kidney allergy in their clinical history (patient 1). In agreement with our data from the structured interviews, in these patients, the mean time between OCT and elicitation of allergic symptoms was 10 hours; in patients with a history of additional red meat allergy, it was 2.42 hours. Both patients with allergy to only pork kidney (patients 2 and 4), who underwent OCT with mammalian meat, did not react, even after application of cofactors such as acetylsalicylic acid (ASS) or alcohol. In contrast, 2 patients with additional red meat allergy in their history (patients 3 and 5) displayed allergic symptoms upon OCT combined with cofactors. Interestingly, patient 5 also reacted in OCT with beef meat and gelatin, but not with deer meat.[7] Oral allergic symptoms were never observed during any of the OCT. Consequently, based on diagnostic measures including OCT, an individual risk assessment was made. However, it needs to be emphasized that OCT, even including cofactors, is still an estimate of reactivity. The probability to react might change according to exposure and additional boosts, such as tick bites.[8,9]

As demonstrated, the reactivity in skin tests with fresh meat or gelatin in this study seems to reflect the content of accessible α-Gal epitopes in these preparations (Fig 1). Unfortunately, skin