negative, including those related to the episode. A positive skin test was defined for a minimum wheal diameter 3 mm larger than the negative control.

Total and specific immunoglobulin E (IgE) were measured by ImmunoCAP (Thermo Fisher Scientific). Specific IgE was repeatedly negative for seminal fluid extract (0.02-0.08-0.01 kU_A/L). Specific IgE measurements were positive for: dog dander, 17.8 kU_A/L; dog prostatic kallikrein (Can f 5), 27.70 kU_A/L; *Olea europea* pollen, 8.57 kU_A/L; latex, 7.5 kU_A/L; Hev b, 6.01 20.30 kU_A; Heb v 6.02 19.50 kU_A/L; and negative (<0.35 kU_A/L) for dog lipocaline and other latex components. Total IgE was above normal levels (1,330 kU/L). Baseline serum tryptase was within normal levels (5.4 μg/L).

Basophil activation test (BASOTEST, Beckton-Dickinson), performed with 2 dilutions (1:100 and 1:10) of seminal fluid, was positive (stimulation index 58.63, basal stimulation 1.05%), while negative in 2 healthy controls.

Sodium dodecyl sulfate polyacrylamide gel electrophoresis immunoblotting performed with the spouse's seminal fluid for detection of IgE-binding proteins in the patient's serum was negative in reducing (with 2-mercaptoethanol) and nonreducing conditions (without 2-mercapthoetanol).

The inhibition of the patient-specific IgE binding to dog prostatic kallikrein (Can f 5) (ImmunoCAP, Thermofisher) with the spouse's seminal fluid was negative.

This is to our knowledge the first reported case of a systemic anaphylactic reaction after anal intercourse, with good tolerance of the vaginal route and without evidence of an IgE-mediated mechanism.

Based on the medical history and in vivo test results, the patient was diagnosed with hypersensitivity to seminal fluid. This diagnosis was supported by the intense positivity of specific IgE for dog kallikrein,[4] which is cross-reactive with human prostate specific antigen, the main allergen in human seminal fluid.[5] However, we failed to detect specific IgE for seminal fluid antigens. Moreover, the inhibition assay of the patient-specific IgE binding to dog prostatic kallikrein, with the spouse's seminal fluid, gave a negative result. Alternative explanations for anaphylaxis as food allergy or latex exposure were discarded.

The confounding results of the allergy evaluation make the reported case exceptional. We wonder whether similar cases occur, but only those with identification of an IgE mechanism are published.[1,6]

We ruled out the diagnosis of postorgasmic illness syndrome, characterized by transient flu-like symptoms and cognition symptoms. This condition is infrequent in women, and the patient showed no symptoms related to vaginal intercourse.[7]

We hypothesized that tolerance to seminal fluid exposure by vaginal route may be explained by 3 circumstances: 1) The reaction presented was attributable to other components (enzymes and other mediators) present in the seminal fluid,[8] responsible for local symptoms as well as positive results when performing skin and basophil activation tests; 2) The slightly acidic vaginal pH[9] could influence the biological effect of seminal fluid (the human prostatic kallikrein is a basic protein that may become neutralized by the vaginal acid pH). In fact, reports have been made of women sensitive to seminal fluid complaining of local symptoms after vaginal intercourse[10]; 3) The anal area is highly irrigated by the hemorrhoid plexus, which facilitates local absorption.

We conclude that in a case of anaphylaxis after sexual intercourse, the diagnosis should address the identification of sensitivity to seminal fluid components. However, a non–IgE-mediated mechanism may be involved. The composition of seminal fluid and the route of exposure may play a role.

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Improved patient adherence to subcutaneous allergen immunotherapy using a modified rush immunotherapy protocol

Despite the efficacy of allergen immunotherapy (AIT), studies demonstrate low compliance rates.[1] Adherence during buildup is especially challenging for patients. Rush immunotherapy (RIT) provides a faster method to reach maintenance dose, eliminating several months of buildup, potentially leading to higher patient adherence and accelerated symptom control. Few studies have directly compared the compliance rates of RIT schedules vs conventional schedules in patients from the same office.[2] Safety and increased frequency of reaction rate continue to be primary concerns of RIT.[3] Modified RIT (mRIT), by stopping at a lower target dose, has been shown to decrease systemic reaction rates from 27% to 38% per patient in premedicated RIT[3] to 2% to 28% per patient in premedicated mRIT.[4–7] In some studies, the reaction rates for mRIT protocols are comparable to a conventional buildup, reported as 7% to 12% per patient[8] and 0.2% per injection.

Patients who followed a mRIT schedule, compared with patients receiving conventional buildup AIT, were more likely to adhere to

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Table 1
Modified Rush Immunotherapy Schedule

Dose	Time interval	Volume (mL)	Dilution
1st		0.05	1:10,000
	15 minutes		
2nd		0.2	1:10,000
	15 minutes		
3rd		0.05	1:1,000
	15 minutes		
4th		0.2	1:1,000
	15 minutes		
5th		0.05	1:100
	30 minutes		
6th		0.2	1:100
	60 minutes		
7th		0.05	1:10
	60 minutes		
8th		0.2	1:10
Observation	120 minutes		

the buildup treatment regimen and experience decreased systemic reactions when compared with a standard rush protocol. The goal of our protocol modification was to increase buildup adherence while decreasing the frequency of systemic reaction using an mRIT target dose of 0.2 mL of a 1:10 dilution. The following week, 0.1 mL of a 1:10 dilution was administered. From this dose, patients in both the mRIT group and conventional group followed identical buildup schedules. We defined adherence as ordering a maintenance vial, a concrete outcome measure for completing the buildup phase of AIT. We defined systemic reaction rates according to the World Allergy Organization Subcutaneous Immunotherapy Systemic Reaction Grading System.[9]

This study was a retrospective cohort study of patients older than 12 years of age whose treatment course began in 2014, with buildup extended into 2015, at Grand Rapids Allergy who started subcutaneous AIT with a conventional buildup or modified RIT. Table 1 describes the protocol for our modified RIT. Premedications included second-generation antihistamine, ranitidine, montelukast, and prednisone 2 days before and on the day of the modified RIT procedure. A maintenance dose was defined as 0.5 mL at a dilution of 1:1. Reaching maintenance dose was determined by an order placed for a maintenance concentration vial. Reaction rates were recorded in the modified rush cohort and grading based on the World Allergy Organization Subcutaneous Immunotherapy Systemic Reaction Grading System.[9] Approval to conduct the study was granted by the Michigan State University Institutional Review Board (protocol number x16-1269 and x16-1609).

Summary statistics were calculated for the data. Comparisons between groups for quantitative variables were performed using the t test and are expressed as the mean ± standard deviation. Nominal variables were evaluated using the χ^2 test and are expressed as percentages. Logistic regression was performed. Statistical significance was assessed at $P < .05$.

Data were collected from patients ranging from 12 to 81 years of age. There were 623 eligible subjects, none of which were dropped from the study. A modified rush protocol was selected by 37% of patients. The conventional group included 392 subjects, with a mean age of 36.9 ± 14.2. The modified rush group included 231 subjects, with a mean age of 35.2 ± 17.8 years. No significant difference in age was found between the 2 groups ($P = .212$).

Of the 392 subjects in the conventional group, 253 reached maintenance (64.5%), as defined by ordering a maintenance vial. Of the 231 modified rush subjects, 195 reached maintenance (84.4%), a statistically significant difference ($P < .001$) in the proportion of patients who reached maintenance dose between the 2 immunotherapy groups. Those who followed a modified rush protocol were 2.9 times more likely to reach maintenance dose than those who followed a conventional protocol (95% confidence interval [CI], 1.9-4.4). Age at starting dose was also a significant predictor; as age increased, so did the likelihood of reaching maintenance dose (95% CI, 1.01-1.03).

During the modified rush procedure, 24 of 231 (10.4%) patients experienced symptoms of a systemic reaction. Six (2.6%) of these patients reported flushing only. Twenty-one (6.5%) patients experienced grade 1 systemic reactions, and 3 (1.3%) patients developed grade 2 systemic reactions. Five patients required epinephrine during the procedure (2.2%). Age, sex, body mass index, history of asthma, and whether patients were percutaneous positive to common allergens (tree, grass, weed, mold, dust mite, cat, dog) were evaluated as potential risk factors for systemic reaction. None of these were found to significantly predict a systemic reaction.

Our overall goal with a modified RIT protocol was to increase patient adherence by accelerating symptom relief with decreased time to a maintenance dose, while minimizing the risk of systemic reactions. Our reaction rate was comparable to those of other studies evaluating systemic reaction rate from mRIT.[5–7] Systemic reactions were limited to grades 1 and 2, with flushing being the most frequent reported reaction; a similar pattern was seen in a study of RIT to multiple allergens.[8]

A limitation of this study is that we used ordering of the maintenance vial as a surrogate for patient adherence. Possibly, although patients reached the maintenance vial of their therapy, they may not have received continued doses from the maintenance vial. Absolute adherence to AIT, conventional or rush, would require a longer study through 3 to 5 years of immunotherapy.

Additionally, selection bias may be built into the retrospective chart review study design. Patients were offered the option to pursue a modified rush schedule or a conventional buildup schedule when beginning AIT. Patients who choose a modified rush schedule may be inherently different in ways that may confound the study.

Our modified RIT schedule offers a solution that optimizes adherence and safety. In our study, a modified RIT option in an outpatient setting significantly improved adherence, with 84.4% of patients ordering a maintenance vial. Systemic reaction rates were similar to published rates during conventional buildup.[8] With this study, we hope to contribute to a growing body of research leading to incorporation of a modified RIT option to increase adherence for patients choosing to begin immunotherapy.

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