

geometric mean and geometric SD of FeNO levels in the 20 healthy children was 7.0 ppb (SD, 1.52; Fig 1). The geometric mean FeNO level in the 20 children with eczema was 11.7 ppb (SD, 1.71). Statistical analysis using a 2-tailed *t* test comparing the 2 groups showed a statistically significant difference between the 2 groups ($P = .002$; 95% CI for ratio of geometric means, 0.44-0.81). There was no significant correlation between FeNO levels and severity of eczema ($P = .37$), topical steroid use ($P = .53$), and symptoms of allergic rhinoconjunctivitis/positive allergy tests ($P = .56$).

To our knowledge, this is the first study looking specifically at the levels of FeNO in infants and toddlers with eczema. Our study demonstrates that accurate offline sampling of exhaled NO in children as young as 6 months of age is feasible and valid, and serves to establish normative FeNO data on infants and toddlers. In our study, children younger than 3 years with eczema had FeNO levels that were significantly higher than those of healthy control children, before the onset of significant wheezing. Some of the children with eczema had FeNO levels similar to those of children without eczema, whereas a subset had elevated levels. However, unlike the cohort at risk for wheezing in the Prevention of Early Asthma in Kids study that had evidence of aeroallergen/food sensitization and atopy,⁹ we did not find a difference in parameters such as the severity of eczema or presence of allergy that might predict the elevated FeNO among that subset. Notably, the numbers of subjects in the subsets were small, and not all children with eczema underwent allergy testing.

Balboa et al⁶ performed a cross-sectional study of 105 healthy children age 6 to 14 years designed to evaluate FeNO in healthy children and children with asthma and to relate this variable to different treatment regimens. They observed that, depending on the severity of their disease, children with atopic dermatitis had higher FeNO concentrations (23.07 ppb) than those without atopic dermatitis (11.68 ppb; $P < .001$). Franklin et al¹⁰ investigated various methodological issues on tidal breathing FeNO in 88 infants with and without wheeze. They found no significant difference in mixed FeNO between healthy and wheezing children, but children with doctor-diagnosed eczema had significantly raised levels ($P = .014$).

In conclusion, our preliminary study shows that eczematous infants and toddlers <3 years with no previous history of wheezing had FeNO levels that were significantly higher than those of control healthy children. Serial FeNO measurements over time, along with symptom monitoring, may be of potential benefit in predicting the development of asthma in these high-risk children. Early detection of preclinical asthma could open the door to early intervention, such as the use of inhaled fluticasone in the Prevention of Early Asthma in Kids trial.⁹ Larger trials looking at other biomarkers and parameters of atopy may help answer some of these questions in a more definitive manner.

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Prostate-specific antigen as allergen in human seminal plasma allergy

To the Editor:

Human seminal plasma allergy is made up of a spectrum of clinical symptoms caused by local or systemic hypersensitivity reactions after contact with human ejaculate. Symptoms manifest during or soon after sexual intercourse and range from localized vulvovaginal pruritus to life-threatening anaphylaxis.¹

Reactions may have varying origin and are not always referable to true sensitization against allergens present in the seminal plasma. They may also be related to sensitizations against latex (condoms), spermicidal agents (vaginal contraceptives), local anesthetics (in some condoms), or components of lubricants. In addition, there have been

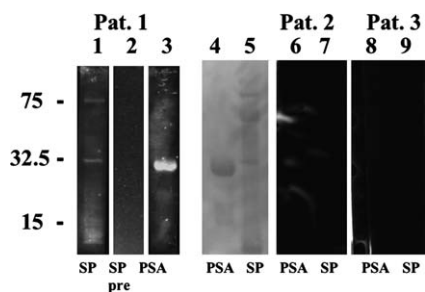


FIG 1. Western blot. *Lane 1 (left):* Western blot detection of a major band at about 33 kD in seminal plasma (SP), which is recognized by an IgE class molecule contained in the patient's serum (dilution 1:5, Pat. 1). A weaker signal of higher molecular weight is likely to represent a dimer; immunoreactive faint bands of 15 kD and less are most likely degradation products. *Lane 2:* Preabsorption of the patient's serum (500 μ L pre) with pure PSA (100 μ g for 2 hours at room temperature) abolished the immunoreactive band. *Lane 3 (right):* Western blot detection of purified PSA by an IgE class molecule contained in the patient's serum (diluted 1:5). Experiments were repeated several times, using 2 different seminal plasma samples of the husband and 2 serum samples obtained from the patients at different time points. *Lanes 4-9:* Control experiments using sera from a healthy donor (Pat. 2, lanes 6 and 7) and from a donor with pollen allergy (Pat. 3, lanes 8 and 9). *Lanes 4 and 5* show a Ponceau protein stain of the samples probed with either serum, namely purified PSA (lane 4) and seminal plasma (SP; lane 5) of the husband. Note absence of any immunoreactive bands, indicating lack of any IgE molecules that recognize PSA in either donor. Pat., Patient; pre, preabsorption.

single reports describing anaphylactic reactions after exposure to ejaculate in women with strong sensitizations to particular allergens—for example, drugs such as thioridazine, penicillin, and vinblastine; or food such as walnuts or food components such as in Coca-Cola (The Coca-Cola Company, Atlanta, Ga)—which had been taken up by the sexual partner and had obviously been transferred by seminal plasma.¹

Most of the women showing allergic reactions to seminal plasma are 20 to 30 years of age and have atopic diseases such as allergic rhinoconjunctivitis or exhibit a positive family history of atopy.¹

In the majority of cases, symptoms arise after their first sexual intercourse and may gradually worsen after several times of sexual intercourse. In these cases, hypersensitivity to seminal plasma appears not to be confined to a particular male sexual partner.¹ Although specific IgE antibodies to seminal plasma are frequently found in cases of seminal plasma allergy, there is no coherent information concerning the precise characterization and origin of allergens responsible.¹

Here we present the case of a 31-year-old woman with a 2-year unfulfilled desire for children, who complained about recurrent rhinitis, asthma attacks, and conjunctivitis 30 to 45 minutes after sexual intercourse. The patient had a 10-year history of asthma with multiple sensitizations against aeroallergens, which had been treated with antihistamines and inhaled steroids. In addition, she had sensitization to latex.

The couple had a 6-year-old daughter conceived through *in vitro* fertilization (fifth cycle), which had been

performed because of reduced quality of the husband's semen (sperm concentration, $2.2\text{--}12.5 \times 10^6/\text{mL}$; WHOa motility, 20% to 30%; normal sperm morphology, 10% to 20%).

Sexual intercourse-related symptoms had started after the birth of the daughter and 2 years before admission, and could be prevented by the use of latex-free condoms. Precoital application of oral glucocorticosteroids showed no benefits.

Physical and routine laboratory examination on admission revealed an otherwise healthy patient. Routine allergy diagnosis using a large panel of aeroallergens and food allergens showed positive skin prick test (SPT) reactions and serum specific IgE (CAP-FEIA; Pharmacia, Uppsala, Sweden) to grass, mugwort pollen, celery, cat, and latex (CAP-classes ≥ 2) as well as seminal plasma (CAP-class 2). Total serum IgE was 1412 kU/L. Further SPTs showed positive reactions to 1:2, 1:4, 1:16, and 1:160 dilutions of her husband's seminal plasma with PBS, but not to the spermatozoa.

Because the couple wanted to achieve normal sexual relations without the use of condoms, immunotherapy was offered. Subcutaneous desensitization is recognized as the gold standard for the treatment of patients with seminal plasma allergy but is very time-consuming and requires fractionation of whole seminal plasma to obtain the relevant seminal plasma proteins and to remove proteins known to interfere with successful desensitization.² Because the couple refused this procedure, an intravaginal rush desensitization was attempted using 2 mL of 10^{-5} diluted husband's seminal plasma with 10-fold increments in concentration to undiluted semen at 20-minute intervals.³ Thereafter, the patient had repeated unprotected sexual intercourse at intervals of 2 to 3 days with slight local itching and vulvar swelling only. However, 2 weeks after the desensitization attempt, the patient experienced generalized urticaria with respiratory distress and dizziness 30 minutes after unprotected sexual intercourse with subsequent emergency treatment (dimetindene, prednisolone, and epinephrine). Reactions to food or medication could be ruled out. Serum specific IgE against seminal plasma had increased to 4.27 kU/L (CAP-class 4), and positive SPT reactions against seminal plasma could be observed up to a dilution of 1:10,000.

To examine whether and which components of the husband's seminal plasma were recognized by IgE antibodies of the patient, we performed SDS-PAGE followed by Western blotting (performed with minor modifications as described⁴). Briefly, 30 or 60 μ g seminal plasma were electrophoretically separated on 15% gels and blotted onto nitrocellulose membranes. Membranes were incubated with serum of the patient (1:5 to 1:50 dilutions). As a second antibody, horseradish peroxidase-coupled goat-antihuman-IgE antiserum (1:1000; Bethyl Laboratories, Montgomery, Tex) was used, followed by chemiluminescence detection. A clear band of about 33 kD was visible, suggesting that prostate-specific antigen (PSA) may be recognized by the patient's IgE. Indeed, commercial, highly pure human PSA (5 μ g/lane; HyTest Ltd, Turku, Finland) used subsequently also yielded a strong band when probed with the patient's serum. After preabsorption

of the patient's serum with pure PSA, the immunoreactive bands were absent. Furthermore, when serum from a healthy female or from a female with pollen allergy was used instead of the patient's serum, neither pure PSA nor PSA in seminal plasma was recognized (Fig 1). Together, these results strongly suggest that PSA was selectively recognized by IgE antibodies contained in the patient's serum.

A cellular allergen stimulation test (CAST; Bühlmann Laboratories, Schönenbuch, Switzerland) yielded positive results with high leukotriene release after incubation with husband's seminal plasma diluted 1:10 to 1:160, and with PSA 0.04, 0.02, and 0.01 $\mu\text{g/mL}$, whereas no reactivity was seen in 3 healthy controls. Furthermore, quantitative determination of *in vitro* basophil activation performed with the Basotest kit (Orpegen Pharma, Heidelberg, Germany) showed more than 50% basophil activation after incubation with all dilutions (1:10 to 1:160) of the husband's seminal plasma as well as PSA, whereas basophils from the normal subjects were unreactive (Fig 2). The description of both techniques has recently been published in detail.⁵

The nature of human seminal plasma allergens has been unknown so far, but results from previous studies suggested that the site of origin might be the prostate.¹ In the current case, for the first time, PSA could be identified as the causative allergen as strongly indicated by positive SPT, immunoblotting, cellular antigen stimulation, and basophil activation testing.

Prostate-specific antigen is well known as a marker for detection and management of prostate cancer⁵; it is the most abundant protease in human seminal plasma, where it functions to degrade high-molecular-weight proteins synthesized in the seminal vesicles. In prostate tissue and in seminal plasma, PSA predominantly exists in a free form as a noncomplexed 33-kd protein consisting of a single polypeptide chain of 240 amino acids, whereas in serum, PSA is present mainly in a complex form with protease inhibitors such as α_1 -antichymotrypsin.⁶

The findings in the presented case report are in line with previous studies performed before limitations caused by HIV and ethical limitations, which could demonstrate positive SPT reactivity in sensitized women against seminal plasma of different men but not other species⁷ and against expressed prostatic secretions and prostatic tissue extractions.⁸ In addition, in early chromatographic investigations, 90% of the allergenic activity of human seminal plasma was found in fractions with a molecular mass between 12 and 75 kd,⁶ and allergenicity is not modified after vasectomy.⁹

In the presented case, intravaginal desensitization using the husband's whole seminal plasma failed. Graded intravaginal challenges have been shown to be less effective as traditional subcutaneous desensitization, but have been recommended as first therapeutic approach before pursuing subcutaneous desensitization because they are less time-consuming and easier to administer.¹⁰ It might be speculated whether in the presented patient successful desensitization could be achieved by using purified PSA obtained from the husband's seminal plasma or serum.

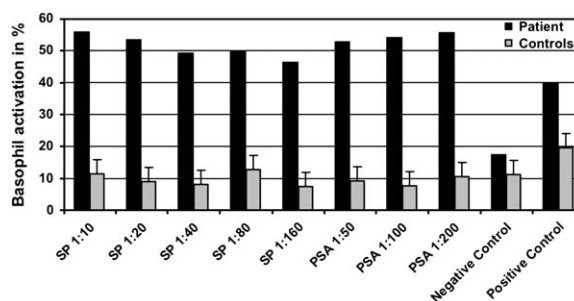


FIG 2. Basotest. Mean basophil activation (percentage of CD63⁺ basophils) and SD in the patient and 4 healthy controls after incubation with seminal plasma (SP) up to a dilution of 1:160 and PSA 0.04, 0.02, and 0.01 $\mu\text{g/mL}$.

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Asthma attacks induced by low doses of celecoxib, aspirin, and acetaminophen

To the Editor:

Coxibs are a new class of potent nonsteroidal anti-inflammatory drugs that selectively inhibit the COX-2