



## Anaphylaxis and Human Seminal Plasma Allergy: A Review

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### Abstract

Allergy can be defined as a detrimental immune-mediated hypersensitivity response to common environmental substances. The immune processes of allergy usually rely on the production of IgE antibodies specific to common allergens. Anaphylaxis is usually considered an acute, severe reaction, often with dyspnea, angioedema, and hypotension. The manifestation of allergic diseases changes throughout life: food allergies and eczema are most likely to develop in infants, asthma in young children, and rhinitis in older children and adults. Human seminal plasma allergy is an anaphylaxis caused by immediate hypersensitivity to human seminal plasma. Immediate hypersensitivity reactions to human seminal fluid range from local swelling to generalized systemic reactions. Allergy to human seminal plasma is a rare condition and therapeutic options include the use of condoms, prescription of antihistamines and attempts at desensitization. The incidence of this allergy is higher than reported due to lack of recognition and hence early detection will enable the physician to direct an appropriate therapy. The present review focuses on clinical features, diagnosis and therapy of seminal plasma allergy.

**Key words:** Allergy, Anaphylaxis, Genital allergy, Human Seminal Plasma, Hypersensitivity,

### Introduction

Allergy can be defined as a detrimental immune-mediated hypersensitivity response to common environmental substances. The immune processes of allergy usually rely on the production of IgE antibodies specific to common allergens. <sup>[1]</sup>

The first time a body is exposed to an allergen, the T-cells, specifically T-helper-2 (TH2) cells, initiate the allergic reaction by releasing interleukine-4 and interleukine-13 (IL-4,IL-13),

which activate and induce proliferation of the B-cells, which then produce the antigen specific Ig-E. There is a cross-link between multivalent antigen and basophils or mast cells by Ig-E specific for that antigen which leads to the degranulation of basophils and mast cells and release of inflammatory mediators such as Histamine, eosinophilic chemotactic factor, leukotrienes, prostaglandins, thromboxane A<sub>2</sub>, and platelet activating factor, bradykinins, tumor

necrosis factor-alpha, IL-4, IL-5, IL-6, and IL-13. As the result, these chemicals lead to bronchospasm, hypersecretion of mucus glands, increased capillary permeability and other inflammatory reactions [2].

Anaphylaxis, a form of hypersensitivity reaction (allergy) is derived from the Greek words *a-* (*against*) and *-phylaxis* (*immunity, protection*) [3,4]. Anaphylaxis is usually considered an acute, severe reaction, often with dyspnea, angioedema, and hypotension [5]. Food, venom, and drugs are the most common exogenous antigens that can cause an immunoglobulin E (IgE)-mediated Reaction [6]

The manifestation of allergic diseases changes throughout life: food allergies and eczema are most likely to develop in infants, asthma in young children, and rhinitis in older children and adults [1]. It consists of some or all of the following signs and symptoms: diffuse erythema, pruritus, urticaria, and/or angioedema; bronchospasm; laryngeal edema; hyper peristalsis; hypotension; and/or cardiac arrhythmias. Other symptoms can occur, such as nausea, vomiting, lightheadedness, headache, feeling of impending doom, and unconsciousness [7].

There are several types of specific allergy tests. Immediate type hypersensitivity (IgE) skin tests are typically used to test for airborne allergens, foods, insect stings, and penicillin. Immediate-type hypersensitivity also can be evaluated through serum IgE antibody testing called radio allegro sorbent testing (RAST). Delayed-type hypersensitivity skin tests (patch-type skin tests) are commonly used in patients with suspected contact dermatitis [8]. Human seminal plasma allergy is an anaphylaxis caused by immediate hypersensitivity to human seminal plasma [9]. Immediate hypersensitivity reactions to human seminal fluid have been increasingly recognized and documented. However, no accurate data on the prevalence of such reactions are available, although the disorder appears to be more common than previously believed [10].

Genital hypersensitivity reactions may be subdivided into those that are related to sexual “activity” (for example, kissing, foreplay, coitus) and those that may occur in the absence of sexual contact [11].

### Human Seminal Plasma Allergy

Hypersensitivity to human seminal plasma is defined as a spectrum of systemic and/or localized symptoms after exposure to specific protein components in seminal plasma [9]. Seminal plasma hypersensitivity is an IgE-mediated allergic reaction to specific components of seminal plasma, most likely, prostate glycoproteins, prostate-specific antigen (PSA), a kallikrein with serine-protease activity rather than spermatozoa [12,13].

In 1958, Specken [14] reported the case of a 65 year old woman who suffered post-coital generalized urticaria at times accompanied by bronchospasm. This was the first description of hypersensitivity to semen and over subsequent years a number of cases and series of cases have appeared in the medical literature [15].

Women aged 20 – 30 years are most affected, displaying symptoms immediately or up to 1 h after exposure [16].

In some cases, hypersensitivity reactions to seminal plasma have occurred after an intercourse-free period, such as after pregnancy, hysterectomy, menopause, or partial prostatectomy in the partner.

### Clinical Features

Immediate hypersensitivity reactions to human seminal fluid range from local swelling to generalized systemic reactions [17]. Local reactions include itching, erythema and oedema in the vulvar region, or other areas, which have been in contact with semen. Systemic reactions include dyspnoea, dysphagia, rhinoconjunctivitis, generalised urticaria, angioedema gastrointestinal symptoms, and exacerbation of atopic eczema [16,18]

## Diagnosis

The diagnosis is based on the medical history in combination with avoidance of symptoms by correct condom usage and conventional tests of IgE-mediated allergy<sup>[19]</sup>. Condom test can be diagnostic by demonstrating that symptoms of seminal fluid allergy can be abolished with condom usage<sup>[20]</sup>. Possible sensitizations to other antigens (latex, lubricants, or contraceptives) also should be evaluated<sup>[21]</sup>. Differential diagnosis includes contact dermatitis, candida or bacterial vulvovaginitis, coitus-linked asthma, 'honeymoon rhinitis, anxiety, irritant reactions or latex allergy<sup>[18,21,22]</sup>. However, *in vivo* skin tests are the most important for the diagnosis<sup>[18]</sup>. For skin testing, the first step is to obtain a fresh ejaculate from their husbands or sexual partners. The sample needs to be liquefied at room temperature for 30 min, and then centrifugation is to be carried out to separate spermatozoa and seminal plasma<sup>[22]</sup>.

*In vitro* measurements for specific IgE antibody include radio allegro sorbent tests and enzyme-linked immune sorbent assays<sup>[23,13]</sup>.

Commercial kits for specific IgE tests are available, but their clinical utility is still uncertain<sup>[22]</sup>. Identification of allergens can be performed by electrophoresis, chromatographic separation and IgE immune blotting assays<sup>[20,21,24,25]</sup>.

Several seminal plasma allergens have been characterized and it has been suggested that 14~75 kDa proteins of seminal fluid could be the IgE binding components<sup>[17,26,27]</sup>.

## Management:

Therapeutic options include the use of condoms, prescription of antihistamines and attempts at desensitization. Avoiding the allergen either by abstinence or with condom use is the best option, but this is not always acceptable for patients and their partners. There have been some reports of the prophylactic use of antihistamines (H1 and H2 antagonists) prior to coitus relieving some local symptoms<sup>[28]</sup>. However, recent studies have reported that antihistamines can have adverse effects on ovulation<sup>[29]</sup> and embryo implantation

<sup>[30]</sup> in animal models. The effects of antihistamines on human fertility have yet to be examined in any detail.

However, in cases hoping for pregnancy, desensitization can be considered as a useful treatment option. Various immunotherapy protocols have been tried since the first report in 1967 by Halpern et al.<sup>[14]</sup>. Rush immunotherapy protocols have been also performed successfully by subcutaneous or intravaginal route<sup>[31,32]</sup>.

Following desensitization, a regular schedule of sexual intercourse or exposure to human seminal plasma needs to be maintained every 2-3 days to continue tolerance status<sup>[22]</sup>. Artificial insemination is also another proposed option for cases hoping for pregnancy.

In 1981, Shapiro et al<sup>[33]</sup> reported the first successful induction of pregnancy after artificial insemination in a woman with human seminal fluid allergy.

Another case of successful pregnancy after artificial insemination with sperm devoid of seminal plasma proteins was described by Iwashashi et al<sup>[34]</sup>. In both cases, more than 4 cycles of insemination were required.

## Conclusion

Seminal plasma allergy is a relatively rare condition. However, it has been suggested that the incidence of human semen allergy is probably higher than reported because of lack of recognition in the medical community and underreporting by patients. Seminal allergy should therefore be considered a possible cause in women complaining of local and/or systemic symptoms after coitus, especially if the symptoms are not experienced with condom use. Diagnosis of the allergy should be done by an appropriate tool which may require collaboration with a clinician trained in allergy department.

Once an allergen is identified, avoidance or abstinence is the main stay of therapy. However desensitization or artificial insemination can be other alternatives in cases hoping for pregnancy.

Recognizing this condition early will enable the clinician to direct appropriate therapy.

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