

DR. MARK HOLBREICH (Orcid ID : 0000-0002-5902-2584)

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## Features of Food Induced Immediate Response in the Esophagus (FIRE) in a Series of Adult Patients with Eosinophilic Esophagitis

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### To the Editor

Eosinophilic esophagitis (EoE) is a chronic inflammatory disease characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil predominant inflammation. The leading symptom in adults with active EoE is solid food dysphagia. A quantitative tool has been developed to characterize the nature of these symptoms (1). Most typically patients complain of food going down slowly, food getting stuck and pain. These symptoms are most likely to occur during the passage of dense solid foods such as meats, bread and rice and are temporally limited to the passage of foods.

Recently a phenomenon with a different symptom referred to as FIRE (food induced immediate response in the esophagus) has been described in adults with EoE. (2). Patients with eosinophilic esophagitis describe these esophageal symptoms as clearly distinct from dysphagia. The symptoms typically occur rapidly after the food has come in contact with the esophageal surface and is often described as tightening or pressure but without the sense of dysphagia. A large series of Swiss patients with eosinophilic esophagitis were queried via a form mailed to their homes or in clinics

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concerning symptoms related to an immediate response in the esophagus distinct from dysphagia (2). A significant portion (49%) reported some form of esophageal discomfort related to eating. Although certain subject characteristics in this study such as younger age of onset of EoE and higher prevalence of allergies was noted, detailed clinical information on each subject was not available for review. Here in we describe a series of patients with biopsy proven eosinophilic esophagitis who identify characteristic symptoms of FIRE following a specific food ingestion. For each selected FIRE patient a detailed chart review was conducted characterizing their demographics and EoE history (Table 1) as well as characteristics of their FIRE profile (Table 2). A number of features were noted in this group of 8 EoE patients with FIRE symptoms. The onset of symptoms most often occurred within 1-60 minutes (median 3.5 minutes) after ingestion of the food. The duration of symptoms lasted from <10 minutes to > 6 hours (median 120 minutes). Among the patients the description of discomfort was often similar consisting of a tightening or pressure in the mid sternum. Subjects were questioned carefully to distinguish FIRE symptoms that occur quickly after ingestion from symptoms typically associated with gastroesophageal reflux. The most common foods inducing symptoms were beans, melon and craft beer. The symptoms were significant enough that patients attempted to subsequently avoid these foods. Six patients (75%) had coexisting pollen food allergy syndrome (PFAS). All patients were questioned in detail and they were able to distinguish between symptoms related to their pollen food allergy syndrome and FIRE.

The exact mechanism of this esophageal discomfort has so far not been elucidated. It appears distinct from pollen food allergy syndrome based on its distinct uncomfortable symptoms localized in the esophagus. Pollen food allergy syndrome is characterized by itching of the oral mucosa upon contact with fresh fruits or vegetables. It also appears different from EoE as uncommon foods such as banana, melon and avocado were capable of invoking symptoms, notably foods more commonly associated with pollen food allergy syndrome. However the strong association with atopy, the rapid onset of symptoms and symptoms distinct from dysphagia suggest a local possibly immunologic factor causing an immediate esophageal mucosal response. A careful history of FIRE symptoms

should be part of the routine history of patients with eosinophilic esophagitis. Additionally a history of IgE-mediated food allergies, allergic rhinitis and pollen food allergy syndrome should be obtained. Further investigations will be required to help better understand the frequency and mechanism of this newly described phenomenon.

1. Schoepfer AM, Straumann A, Panczak R, et al. Development and validation of a symptom-based activity index for adults with eosinophilic esophagitis. *Gastroenterology* 2014;147:1255–1266.
2. Biedermann, L, Holbreich, M, Atkins, D, et al. Food-induced immediate response of the esophagus—A newly identified syndrome in patients with eosinophilic esophagitis. *Allergy*. 2020; 00: 1– 9.

Mark Holbreich M.D.

Allergy and Asthma Consultants

Indianapolis IN USA

Alex Straumann M.D.

Head of Swiss EoE Clinics and Research Network

Department of Gastroenterology and Hepatology

University Hospital Zurich

Zurich, Switzerland

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Corresponding author

Mark Holbreich M.D.

Allergy and Asthma Consultants

8902 N Meridian Street

Indianapolis IN USA

mholbreich@comcast.net

Table 1 FIRE Patient Characteristics

| Patient                     | 1               | 2          | 3          | 4    | 5                 | 6    | 7              | 8    |
|-----------------------------|-----------------|------------|------------|------|-------------------|------|----------------|------|
| Age (yrs.)                  | 19              | 39         | 35         | 53   | 19                | 37   | 28             | 53   |
| M/F                         | M               | M          | M          | M    | M                 | M    | M              | F    |
| AR+                         | PAR             | SAR        | SAR        | PAR  | PAR               | PAR  | PAR            | SAR  |
| Asthma                      | Y               | N          | N          | Y    | Y                 | N    | N              | N    |
| Anaphylaxis<br>++/food      | M,E,P,TN        | P,TN       | P          | None | P,TN              | P,TN | None           | None |
| PFAS +++/food               | Apple<br>banana | All fruits | All fruits | N/A  | Carrot<br>avocado | N/A  | Pea<br>poultry | Soy  |
| EoE sx<br>duration(yrs.)    | 9               | 25         | 20         | 20   | 5                 | 16   | 10             | 5    |
| Time to<br>diagnosis (yrs.) | 1               | 18         | 14         | 18   | 5                 | 1    | 1              | 4    |
| Impactions                  | 0               | 2          | 0          | 0    | 1                 | 0    | 0              | 0    |
| Dilations                   | 0               | 0          | 2          | 5    | 0                 | 10   | 1              | 1    |

+Skin test documented environmental allergies: AR (allergic rhinitis), SAR (seasonal allergic rhinitis), PAR (perennial allergic rhinitis)

++ Skin test documented history of IgE mediated food anaphylaxis: M: cow's milk, E: egg, P: peanut:  
TN: tree nut

+++Pollen Food Allergy Syndrome

Table 2 FIRE PROFILE

| Patient                  | 1        | 2          | 3         | 4          | 5                 | 6          | 7              | 8    |
|--------------------------|----------|------------|-----------|------------|-------------------|------------|----------------|------|
| Chest Symptom            | cramping | tightens   | tightness | tightness  | tightness         | pain       | pressure       | pain |
| Severity +               | 7        | 7          | 6         | 5          | 8                 | 8          | 6              | 8    |
| Time to onset (min)      | <1       | <5         | <2        | <60        | <1                | <10        | <2             | <10  |
| Duration (min)           | <30      | <120       | <120      | <360       | <120              | <360       | <10            | <120 |
| Identified food(s)       | soy      | melon      | beans     | Craft beer | avocado<br>banana | Craft beer | Beans<br>melon | soy  |
| PST++ to identified food | POS      | Not tested | POS       | Not tested | Not tested        | Not tested | POS            | POS  |

+ Analog scale 1-10

++ Prick Skin Test