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POINT OF VIEW

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## Criteria for the suspicion and diagnosis of acute food protein-induced enterocolitis syndrome

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suspicion

### Introduction

Over the past decades, several panels of criteria have been proposed for the diagnosis of acute food protein-induced enterocolitis syndrome (FPIES).<sup>1-5</sup> However, none of them have been validated by a prospective study. Such a study is not easy to carry out, because even the children who most of us would certainly believe to be suffering from acute FPIES, possibly serious, should be subject to oral food challenge (OFC). Moreover, the presence of different phenotypes of the acute FPIES<sup>6, 7</sup> may mean that some of them do not fit into any of the above criteria panels. Particularly, Vazquez-Ortiz et al.<sup>8</sup> reported that milder cases (1/4 in their Southern European cohort) might not be captured by the 2017 Consensus diagnostic criteria,<sup>5</sup> which are the most shared till date. Those authors,<sup>8</sup> as well as all interested researchers, claim for accurate diagnostic biomarkers which, however, are not available at the moment.

### Proposal of new criteria

If to all this (no validation of criteria panels, various phenotypes of acute FPIES, and no highly predictive biomarker), we add the relative aspecificity of the signs and symptoms of acute FPIES, I believe that an anamnestic diagnosis of acute FPIES should be rigorous and conservative on the one hand, to be as specific as possible, and with a high degree of suspicion on the other, for maximum sensitivity.

So, I propose a division (see [Table 1](#)) into:

- anamnestic diagnosis of certainty of acute FPIES;
- anamnestic diagnosis of suspicion of acute FPIES.

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**Table 1** Diagnostic criteria for acute food protein-induced enterocolitis syndrome.

**Anamnestic diagnosis of certainty** (oral food challenge-OFC, is not required for diagnostic confirmation) The following criteria must all be present:

- Repetitive and projectile vomiting arising 1-4 hours after food intake
- Pallor and/or lethargy
- Resolution of symptoms within 6-8 hours after onset (except for possible diarrhoea which could last up to 24 hours)
- Absence of immunoglobulin E (IgE)-mediated like skin and/or respiratory manifestations
- At least two episodes characterized as above
- Absence of ingestions without adverse reactions of the guilty food after the first episode

**Anamnestic diagnosis of suspicion** (OFC is necessary to reach a diagnosis of certainty, in the meantime the suspected food must be excluded from the diet).

It applies in case one of the following clinical scenarios is fulfilled:

- Only one episode of repetitive and projectile vomiting, arising 1-4 hours after food intake, accompanied by pallor and/or lethargy. Skin signs compatible with the suspicion of an IgE-mediated allergic reaction may be present. There should be no ingestion of the same food without adverse reactions after the episode of vomiting.
- At least two consecutive episodes of one (not repetitive) vomit, with or without pallor and/or lethargy, within 1-4 hours after ingestion of the same food. Skin signs compatible with the suspicion of an IgE-mediated allergic reaction may be present. There should be no ingestion of the same food without adverse reactions after the first episode of vomiting.
- At least two consecutive episodes of repetitive vomiting, with or without pallor and lethargy, arising >4 hours after ingestion of the same food. Skin signs compatible with the suspicion of an IgE-mediated allergic reaction may be present. There should be no ingestion of the same food without adverse reactions after the first episode of vomiting.

#### Diagnosis of multiple acute FPIES

For each new suspected food, in a child who has already been diagnosed with acute FPIES, the above suggested criteria for the first food must be applied.

#### OFC modality and positivity criteria

- Administration of a single dose of guilty food (equal to a full serving size for age) and observation for 4 hours.
- Repetitive vomiting arising 1-4 hours after food intake is necessary and sufficient to declare OFC failed. If the vomiting is not repetitive, the OFC will have to be redone. If the second OFC also evokes unrepetitive vomiting, mild FPIES will be diagnosed.
- The administration of ondansetron should be performed after at least 2 vomits.

There are currently no criteria for suspicion for acute FPIES in the scientific literature. In addition, especially for mild forms (but also for very atypical ones), it is necessary to put stakes. Moreover, I propose small variations for the diagnosis of multiple acute FPIES and for the modalities of execution and evaluation of the OFC (see [Table 1](#)).

Vazquez-Ortiz et al.<sup>8</sup> underline that the presence of different phenotypes and in particular the presence of mild forms of acute FPIES lead to misdiagnosis and increased need for costly, potentially risky, food challenges. I believe that today OFC is inevitable to make a correct diagnosis of mild or very atypical phenotypes (for example, with immunoglobulin E [IgE]-mediated like skin and/or respiratory manifestations and/or a time of onset of non-canonical symptoms). Fortunately, the use of ondansetron makes this procedure less risky than in the past.<sup>9</sup>

The association of anamnestic criteria of suspicion plus OFC will allow not to miss the diagnosis of acute FPIES. On the other hand, the assumption of rigorous and conservative anamnestic criteria of definitive diagnosis without OFC will allow assigning an elimination diet only to those who need it.

#### Author contributions

Stefano Miceli Sopo conceived the design of the study, drafted the article, performed, and analyzed the literature search and commented on it. Also, the author revised the article and gave final approval of the version to be published.

#### Declaration of interest

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

I declare that the work described has not been published previously, that it is not under consideration for publication elsewhere, that its publication is approved by all authors and tacitly by the responsible authorities where the work was carried out, and that, if accepted, it will not be published elsewhere in the same form, in English or in any other language, including electronically without the written consent of the copyright holder).

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