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## REVIEW

# Oral immunotherapy for food allergy: A Spanish guideline. Immunotherapy egg and milk Spanish guide (items guide). Part I: Cow milk and egg oral immunotherapy: Introduction, methodology, rationale, current state, indications contraindications and oral immunotherapy build-up phase<sup>☆</sup>



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## KEYWORDS

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## Abstract

**Introduction:** Cow's milk and egg are the most frequent causes of food allergy in the first years of life. Treatments such as oral immunotherapy (OIT) have been investigated as an alternative to avoidance diets. No clinical practice guides on the management of OIT with milk and egg are currently available.

**Objectives:** To develop a clinical guide on OIT based on the available scientific evidence and the opinions of experts.

**Methods:** A review was made of studies published in the period between 1984 and June 2016, Doctoral Theses published in Spain, and summaries of communications at congresses (SEICAP, SEICAP, EAACI, AAAAI), with evaluation of the opinion consensus established by a group of experts pertaining to the scientific societies SEICAP and SEICAP.

**Results:** Recommendations have been established regarding the indications, requirements and practical aspects of the different phases of OIT, as well as special protocols for patients at high risk of suffering adverse reactions.

**Conclusions:** A clinical practice guide is presented for the management of OIT with milk and egg, based on the opinion consensus of Spanish experts.

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## Introduction

Cow milk (CM) and egg are the most frequent causes of food allergy in the first years of life.<sup>1</sup> Two recent European studies conducted by the EuroPrevall group have reported an incidence of CM allergy and egg in the first two years of life of 0.54% (0.57% among the infants recruited in Spain) and 0.84% (0.78% among the infants recruited in Spain), respectively.<sup>2,3</sup> A study carried out in the Valencian Community (Spain), in which the diagnosis was confirmed by oral food challenge, reported an incidence of CM allergy of 0.36% in the first year of life.<sup>4</sup>

The only currently approved treatments for food allergy are avoidance and administration of emergency medications on accidental exposure.<sup>5</sup>

New treatment options have therefore been explored – the most widely studied being oral immunotherapy (OIT). Milk-OIT and egg-OIT induces changes in the immune system and favors the development of desensitization in most patients, though there is little evidence on its long-term safety and efficacy.<sup>6</sup>

Although the immunological mechanisms intervening in OIT have not been fully clarified, this type of therapy is known to induce a decrease in the activation and release of mediators from mast cells and basophils, with an increase in specific IgG4 titers, a decrease in specific IgE levels, the

activation of specific regulatory T cells, and Th2-mediated response inhibition.<sup>7–10</sup> Adverse reactions (AR) are frequent and can also manifest in the maintenance phase. Although such reactions are generally mild, they may prove more serious, with the need for epinephrine administration. While sometimes associated to cofactors (e.g., exercise, infections), AR may appear unpredictably with doses that were previously well tolerated.<sup>5,11</sup>

Desensitization is achieved in most patients, though in at least 20% of the cases OIT fails due to the appearance of AR. For this reason, new therapeutic strategies must be developed, such as for example adjuvant therapy with anti-IgE antibodies, in order to broaden the scope of application of OIT.<sup>12</sup>

The long-term outcome and time needed to achieve permanent tolerance of the causal food are not known.<sup>5,13,14</sup> On the other hand, it must be taken into account that prolongation of the maintenance phase can lead to treatment adherence problems.<sup>15</sup>

These elements of uncertainty are the reason why OIT is currently still advised only in the research setting, not in clinical practice.

However, the fact is that CM and Egg-OIT has already been introduced in clinical practice and forms part of the management options of many hospitals in Spain. Different treatment protocols are being used; it is therefore necessary to define

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