

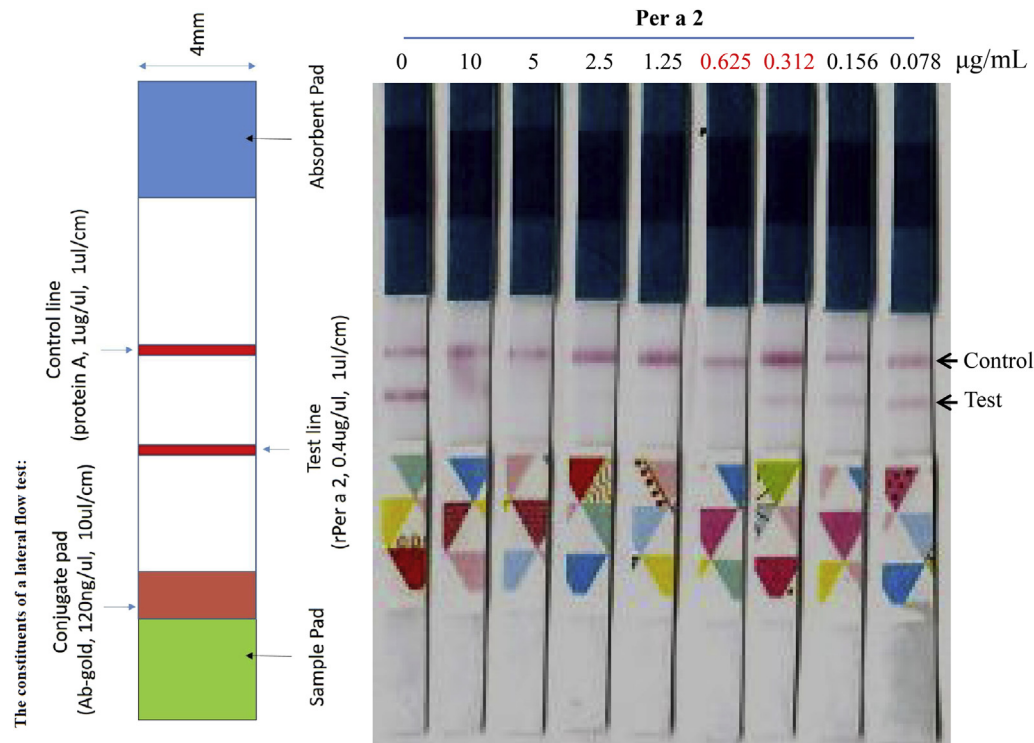


Figure 1. Strip design (left panel) and representative results of test strips detecting Per a 2 in house dust samples (right panel).

simple to use. Using Per a 2, which is a marker allergen for long-term American cockroach control and Per a 9, which is a marker allergen for recent cockroach control, also may give patients and their families more precise information regarding the cockroach levels in their environment, and the effect of any control measures.

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Anaphylaxis due to macrogol in a laxative solution with a positive basophil activation test



Polyethylene glycol (otherwise known as macrogol or PEG) belongs to a family of synthetic nonionic hydrophilic polymers achieved as

condensation products of glycols with ethylene oxide. Different types of macrogol exist, each with a specific molecular weight (from 200 to 20,000 g/mol) and length, which gives them specific pharmacological qualities (eg, viscosity, density). As a consequence, PEG has wide applications as an excipient, solvent, dispersing, and

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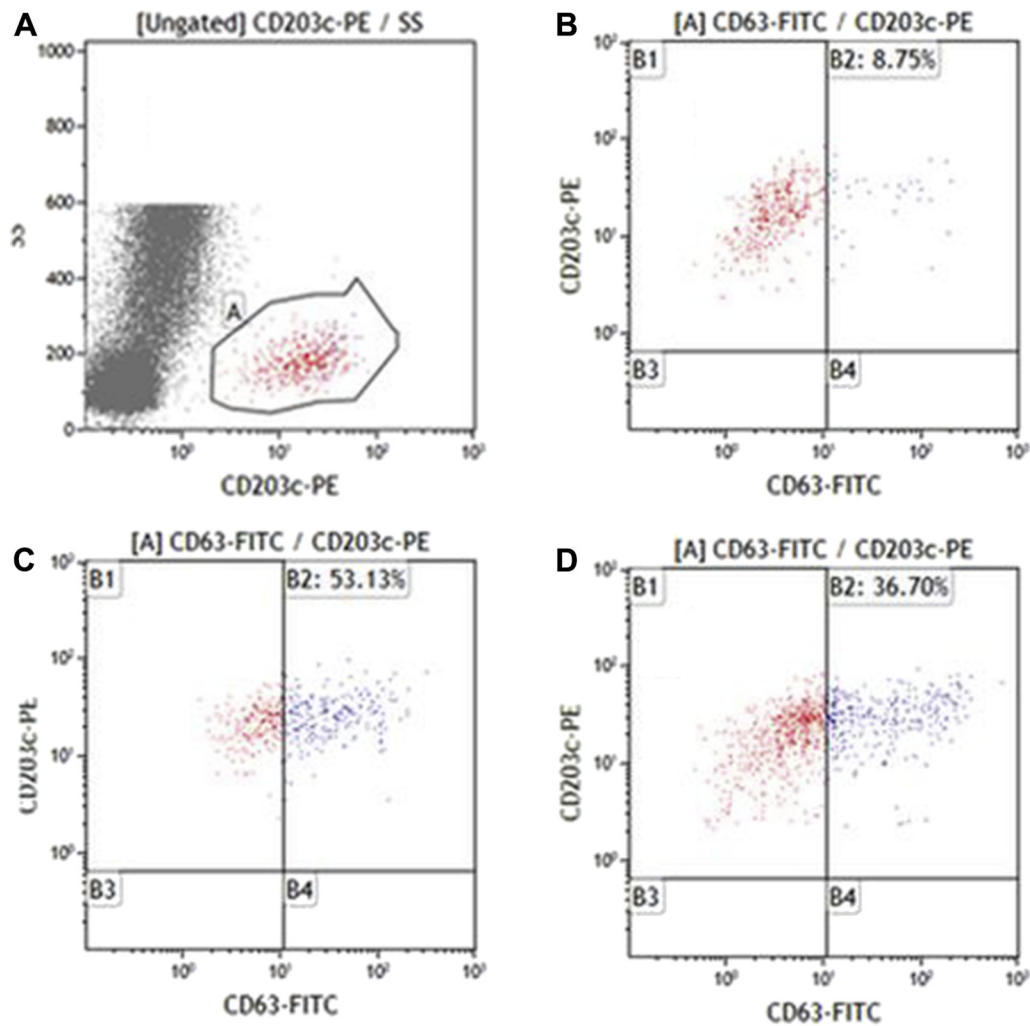


Figure 1. Basophil gating strategy (A). Negative control, degranulation measured by CD63 expression when incubated with PBS-BSA (B). Degranulation when incubated with diluted (1:1000) Bohm (C) and Casenglicol (D), respectively.

thickening agent in the food, cosmetic, medical, and pharmaceutical industries.^{1,2} In particular, macrogol with a molecular mass between 3500 and 4000 g/mol is commonly used as a constituent of laxative solutions. Because of its water binding properties, macrogol is not affected by the intestinal absorption, being able to cross the gastrointestinal tract without going into the systemic circulation, thereby reducing toxicity.³

We report the case of a patient with a history of an immediate hypersensitivity systemic reaction to macrogol 4000 contained in an evacuant solution, together with a positive allergologic study. To our knowledge, this is the first reported case with a positive basophil activation test (BAT) to macrogol 4000 contained in an evacuant solution.

A 65-year-old woman with no previous history of atopy or drug allergy was followed up by the General Surgery and Digestive Department because of colon carcinoma. During a planned admission in the hospital, an evacuant solution (Bohm brand: polyethylene glycol 4,000, KCl, NaCO₃, NaPO₃, NaSO₃, NaCl, neohesperidine, potassic acesulfame, and orange flavoring) was administered in the context of colonoscopy preparation. Previously, she had tolerated evacuant solutions probably containing macrogol. Within a few minutes after the ingestion of the initial dose of this evacuant solution, the patient experienced paresthesia and edema of the lips, malaise, generalized itching, hives, dyspnea, and aphonia. In the physical examination, she

had a generalized pruritic rash and wheezing was heard. Blood pressure was 88/55 mmHg (baseline >140/90), and oxygen saturation was at 95%. She was immediately treated with intramuscular administrations of dexchlorpheniramine (5 mg) and methylprednisolone (125 mg) and showed rapid improvement. Epinephrine was not administered, and serum tryptase was not measured during the reaction.

The patient was referred to our drug allergy unit, and the allergic study was realized 1 month after the reaction. With a detailed anamnesis, we excluded the simultaneous use of other drugs as well as the presence of possible cofactors, such as a concomitant infectious disease. Therefore, we started the allergological investigation with a high suspicion of causality of the evacuant solution. A skin prick test with the same involved laxative solution (Bohm, macrogol 4000, 60 mg/mL) and with another trade name of the evacuant solution with the same molecular weight of PEG (Casenglicol [macrogol 4000, anhydrous sodium sulfate, sodium hydrogen carbonate, sodium chloride, potassium chloride, sodium dihydrogen phosphate]) were performed with positive results (maximum wheals of 7 and 8 mm, respectively). To exclude the possibility of false-positive results caused by irritation effects, skin prick tests with both solutions (Bohm and Casenglicol) were performed in 6 atopic control subjects, with negative results. A CD63 BAT was realized for both macrogol 4000 evacuant solutions, showing positive responses (Fig 1).

To provide the patient with an alternative diagnostic option for the monitoring of her pathology, an oral challenge with a single dose with a “macrogol-free” evacuant solution was performed with good tolerance.

Based on the clinical history and in vivo and in vitro positive results, our patient was diagnosed with an anaphylactic reaction to macrogol (PEG). Subsequently, we advised the patient to check the excipients listed for all kinds of drugs, cosmetics, foods, and other pharmaceutical products that could contain macrogol.

Anaphylactic reactions to macrogol have been rarely reported in the scientific literature. Wenande and Garvey² identified 37 case reports of immediate-type hypersensitivity to PEGs from January 1977 until April 2016.² Therefore, PEG is considered safe and well-tolerated, and consequently, its application has been growing exponentially in multiple fields.^{1–3} In most cases, the described reactions fulfill criteria of anaphylaxis. Despite an intestinal absorption lower than 1% for PEG 3350 g/mol, more than half of reported cases have been described after the administration of laxative solutions,² but specific cases were described with intra-articular, intramuscular, and intravenous injection, and even via topical or vaginal mucosa.^{2,4,5}

Some authors account for the greater frequency of the oral route by citing increased absorption of high-molecular-weight PEG in patients with inflammatory bowel disease and damaged gastrointestinal mucosa.^{1,2} In this way, the loss of the structural or functional integrity is considered a predisposing factor for greater PEG absorption and subsequently sensitization.⁶ The diagnostic workup varies according to the route of administration and the clinical history referred, being the clinical history in many cases the unique tool to deduce an IgE-mediated reaction to PEG.

Both Antón Gironés et al⁷ and Antolin-Amerigo et al⁸ published clinical cases after the use of Bohm evacuant solutions. In contrast with our patient, all patients presented negative results in the skin prick test for PEG 4000, whereas the intradermal test was positive in the group of Antón Gironés et al and negative in the patient described by Antolin-Amerigo et al. Antón Gironés et al performed a single-blind placebo oral challenge, with a positive result in both patients.

Cross-reactivity between PEGs of different molecular weights has been studied. Because of the patient's severe disease, we have not investigated possible cross-reactivity, ignoring possible tolerance to PEG of other molecular weights.

Reviewing the published literature, Bommarito et al⁹ reported a positive BAT after the oral intake of nimesulide granules and paracetamol syrup containing macrogol 4000 and 6000, respectively. Also, Jover Cerdá et al¹⁰ obtained positive BAT response to macrogol

4000 1% and PEG derivatives in a patient who experienced reactions with cough syrup drug, skin cream, and antiseptic containing PEG 6000, PEG-9, PEG-6, PEG-75 and PEG-100, respectively.

In conclusion, we reported a case of anaphylactic reaction to Bohm laxative solution containing macrogol 4000, diagnosed by the clinical history, a positive skin prick test, and BAT to macrogol 4000, suggesting an IgE-mediated immunological mechanism. To our knowledge, this is the first case of systemic hypersensitivity reaction to Bohm laxative solution with a positive BAT for macrogol 4000.

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Immediate vs delayed cow's milk protein allergy in terms of tolerance at year 1

We conducted a trial to compare the rates of positive oral provocation tests (OPTs) and of clinical symptoms present from different systems (gut, skin, respiratory tract) in cases with a positive OPT in a group of immunoglobulin E (IgE) and in 1 of non-IgE cow's milk protein allergy (CMPA) at 1 year of age. Moreover, we tried to identify possible prognostic factors contributing to tolerance at 1 year of age OPT, such as the existence of multiple food allergies, a family history of atopy, the type of milk feeding (breastfeeding vs formula feeding), and the level of antibody concentration against cow's milk protein.

Methods

The study received ethical approval from the Ethics Committee of the Aristotle University of Thessaloniki (Prot. No: 7894). All parents of the participating infants signed written informed consent.

The protocol of the OPT was always starting with a labial challenge followed by gradually increasing doses of 0.1, 0.3, 1, 3, 10, 30, and 100 mL cow's milk (CM) administered with intervals of 20 minutes. In the next day, 3 consecutive doses of 20, 50, and 100 mL CM were administered. Regular assessments were performed to detect symptoms from skin, respiratory, cardiovascular, or gastrointestinal systems. Finally, 100 mL were administered daily from day 3 to day 10 at home.^{1,2}

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