anaphylaxis has been previously reported in just two case reports,[5,10] but desensitisation to ISR to adalimumab has never been reported and, to our knowledge, our case is the first report of subcutaneous desensitisation with adalimumab for ISR.

In conclusion, subcutaneous rapid desensitisation may be a valid alternative for patients with IgE-mediated ISR to adalimumab.

Ethical disclosures

Patients' data protection. Confidentiality of data. The authors declare that they have followed the protocols of their work centre on the publication of patient data and that all the patients included in the study have received sufficient information and have given their informed consent in writing to participate in that study.

Right to privacy and informed consent. Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects mentioned in the article. The author for correspondence is in possession of this document.

Protection of human subjects and animals in research. Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the responsible Clinical Research Ethics Committee and in accordance with those of the World Medical Association and the Helsinki Declaration.

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Long-term selective IgE-mediated hypersensitivity to hydrocortisone sodium succinate

To the Editor,

A clinical problem in patients who have experienced an immediate-type allergic reaction to a medication is represented by how long the persistence of the IgE-mediated allergic sensitisation is. It seems to be different for every drug, ranging from a period of 8–10 years in case of the beta-lactams[1] to up to 29 years for the neuromuscular blockers.[2] Systemic glucocorticoids, as widely reported in literature, can induce immediate-type hypersensitivity reactions,[3] although they are underestimated in clinical practice yet. Currently, the persistence of allergic sensitisation to systemic corticosteroids is unknown, because of the limited number of patients who experience immediate-type hypersensitivity reactions towards these drugs. For that reason, probably, a similar follow-up study has never previously been performed. We observed the case of a patient whose clinical history reported two previous anaphylactic reactions immediately after administration of hydrocortisone hemisuccinate occurred 12 years earlier and who still showed the persistence of serum specific IgE to hydrocortisone.

A 76-year-old female patient not atopic, suffering from chronic bronchitis came to our observation for a bronchial exacerbation with cough and moderate dyspnoea. The

Table 1 Cutaneous test performed with corticosteroids.

Drug	Skin prick test	Intradermal test
Methyprednisolone emisuccinate	10 mg/ml: negative	1 mg/ml: negative 10 mg/ml: negative
Hydrocortisone emisuccinate	10 mg/ml: negative	0.1 mg/ml: negative 1 mg/ml: positive (+ + − −)

patient had also a polyarthrosis, treated with frequent non-steroidal anti-inflammatory drugs (NSAIDs) and analgesics courses. Her medical history stated that facial angio-oedematous reactions appeared after taking various non-steroidal antinflammatory drugs such as diclofenac, ketoprofen, paracetamol. The patient, in addition, had been treated since the age of 44 years with hydrocortisone sodium succinate (HC-SS) intramuscularly as needed, for early menopause and occasional blood hypotension crisis.

In 1997, at the age of 64 years, after the administration of that glucocorticoid, the patient exhibited an anaphylactic reaction with hospitalisation. Few months later, a second anaphylactic episode occurred after a further administration of intramuscular HC-SS. After the acute phase, in an Allergy Unit, the patient underwent an intradermal test (IT) with HC-SS and methylprednisolone sodium succinate (MP-SS) at not specified dilutions with a positive response to HC-SS IT only.

An oral challenge test with nimesulide and an intramuscular challenge test with MP-SS at a dosage of 20 mg were carried out, without eliciting any hypersensitivity reaction. One month later, according to the patient's documentations, another challenge test with HC-SS intramuscularly (10 mg) was carried out, by provoking a generalised urticarial rash a few minutes after steroid administration. The patient tolerated the oral betamethasone and fluticasone via aerosol. Because the patient asked us to investigate her drug hypersensitivity again, we proceeded to perform skin prick tests (SPT) and IT with extemporaneous commercial injectable preparations of MP-SS (Solumedrol 20 mg, Pfizer-Milan, Italy) and HC-SS (Solucortef 100 mg/2 ml, Pfizer-Milan, Italy) diluted in 0.9% saline with different concentrations as shown in Table 1. Positive and negative controls were histamine dihydrochloride, 10 mg/ml and sterile normal saline, respectively. SPT and IT readings were made after 20 min to assess the immediate response. Four patients: two atopic and two non-atopic as healthy controls were enrolled and underwent skin tests with HC-SS and MP-SS at the same concentrations with negative results.

To confirm the reaginic pathomechanism of sensitisation to hydrocortisone, the patient's husband, after giving his written consent, accepted to submit himself to a Prausnitz–Kustner (PK) test with his wife's serum.

The patient's serum was diluted and then 0.1 ml was injected intradermally into the left forearm of the recipient.

48 h later, 0.05 ml of HC-SS (at 1 mg/ml dilution) was injected intradermally at the same site. As negative control, an intrademal test was performed with the same amount of drug on the opposite forearm. The PK test gave positive result with an erythematous wheal (5 mm in diameter) (+ − − −) 20 min after the administration, while no reaction appeared on the opposite forearm. The PK test confirmed the persistence of selective IgE to HC-SS 12 years after her previous anaphylactic reactions. Morning serum cortisol dosage (14.7 mcg/dl – normal range: 6–30 mcg/dl) and serum ACTH (5 pg/ml – normal value: <40.0 pg/ml) were also carried out before administering a slow intravenously incremental challenge test (ICT) with MP-SS (two doses of 5 mg every 30 min followed by 10 mg aft 30 min later and finally 20 mg 12 h later). Since the intravenous ICT with MP-SS gave a negative result, that steroid molecule (20 mg twice/daily) was introduced in patient therapy.

Specific IgE to hydrocortisone and methylprednisolone have been evidenced in vitro by using HC-SS and MP-SS conjugated with human serum albumin,[4] but Japanese authors confirmed the presence of specific IgE to corticosteroids through the use of PK test in two selected subjects belonging to a group of seven patients with asthma who had experienced anaphylactic reactions after systemic corticosteroid administration.[5] In our case, because the composition of the commercial preparations of MP-SS and HC-SS are identical, the tolerability of methylprednisolone intravenously excluded that the patient had produced an IgE-mediated response against the preservative benzyl alcohol, as previously reported by other authors.[6]

A decline in the IgE antibody response has been evidenced for some drugs such as chlorhexidine[7] and penicillins,[1] leading patients to tolerate the drug antigen again,[1] while the persistence of specific IgE to hydrocortisone over time could be due, in our opinion, to the endogenous production of cortisol by the body. Lauerma has previously demonstrated that administration of synthetic ACTH in patients with allergic contact dermatitis to hydrocortisone would result in a reactivation of cutaneous lesions, thus suggesting that T cells of sensitised patients recognise as an allergen either endogenous cortisol or cortisol administered orally as a drug in increasing doses.[8] Since semisynthetic succinated salts steroids undergo hydrolysis in the body, thus allowing steroid molecule bioavailability for its specific receptor,[9] that process could make the drug indistinguishable from the endogenous cortisol amount.

In that way, endogenous cortisol probably contributes to maintain, in our patient, the immunological memory able to induce hydrocortisone specific IgE production, as confirmed by skin tests and PK test. Hydrocortisone allergic sensitisation should be considered lasting lifelong in these patients, but further studies are required to confirm whether such a hypothesis may be applied to other synthetic steroids derived from cortisol.

Ethical disclosure

Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects mentioned in the article. The author for correspondence is in possession of this document.

Confidentiality of data. The authors declare that no patient data appears in this article.

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this investigation.

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Aspirin tolerance following omalizumab therapy in a patient with aspirin-exacerbated respiratory disease

To the Editor,

Aspirin-exacerbated respiratory disease (AERD), also known as aspirin-sensitive asthma, is a clinical entity known as the combination of nasal polyps, asthma, sensitivity to any medications that inhibits cyclooygenase-1 (COX-1) enzymes, namely aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) and chronic hypertrophic eosinophilic sinusitis, as the fourth component recently added. Ingestion of aspirin/NSAIDs results in a spectrum of upper and/or lower respiratory reactions including rhinitis, conjunctivitis and bronchospasm.[1] Anti-IgE mAb omalizumab therapy which is assigned to moderate to severe allergic asthma has recently evolved to be considered in patients with AERD.[2]

We report a 61-year-old woman admitted to the allergy department for uncontrolled severe asthma. She had initially been diagnosed with asthma 35 years ago. She had rhinitis since age 10 and had been operated for nasal polyp at age 20. She was on high-dose inhaled corticosteroid and long acting beta2 agonist combination, montelukast, nebulised salbutamol + ipratropium and fluticasone propionate as needed when she was admitted to our clinic. Although she adhered to the medication regimen she frequently needed parenteral corticosteroids because of poor control of her symptoms. She was admitted to emergency department twice or more times every month due to asthma attacks. On her physical examination bilateral biphasic rhonchi were detected. Pulmonary function test revealed obstructive pattern with fev1: 860 mL (50% predicted). Skin tests with aeroallergens were positive for Dermatophagoides mix and feather mix. Level of total IgE level was 48 IU/mL. She had adverse reaction with the use of aspirin prescribed for cerebrovascular disease two years ago. She had severe dyspnoea 1 h after the first dose of aspirin and she needed treatment in the emergency department. Aspirin therapy was halted thereafter and she was put on clopidogrel therapy instead. A diagnosis of AERD was made based on clinical history. Oral challenge tests with aspirin were planned for definitive diagnosis but was not performed due to the unstable asthma (despite continuous treatment with double doses of formoterol fumarate/budesonide 9/320 μg twice a day, montelukast 10 mg/day and various cycles of systemic corticosteroids) and a FEV1 of 50% of predicted.

In July 2010, she was prescribed omalizumab 150 mg every four weeks (total serum IgE 48 IU/mL, body weight 75 kg) to treat severe asthma symptoms. With the start of omalizumab treatment her symptoms improved