

### Association Between Serum Concentrations of Eotaxin and Testosterone

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Palabras clave: Eotaxina. Quimiocinas. Inmunología clínica. Hormonas sexuales.

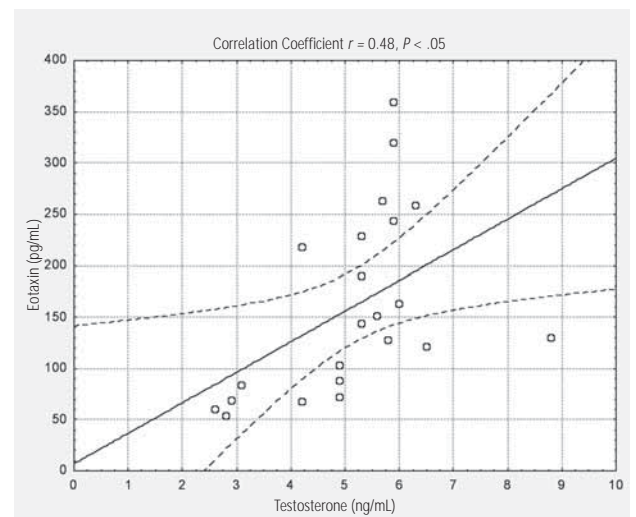
Eotaxin is a highly selective chemoattractant factor for eosinophils and it plays an important role in development of allergic inflammation [1,2]. The association between allergy and sex hormones is still unclear, and an unequivocal interpretation of the influence of sex hormones on the course of allergic symptoms is impossible to make on the basis of present data [3-5]. Previously we proved a significant relationship between serum concentration of eotaxin and the sex and age of healthy and allergic people [6]. The aim of this study was to analyze if there exists a correlation between serum eotaxin and levels of sex hormones in healthy people.

The study group consisted of 38 healthy nonsmokers (16 women and 22 men) aged from 18 to 50 years. Individuals with allergic or neoplastic diseases, immunodeficiencies or endocrinopathies, or those who had had any infectious disease during the last 3 months or had been treated with immunosuppressive, antihistamine or antileukotriene drugs, steroids or other hormones were excluded. Pregnant or postmenopausal women and postandropausal men were also not included. Every subject signed an informed consent form.

In women, serum concentrations of eotaxin and sex hormones were estimated in 3 consecutive phases of the menstrual cycle. The first blood sample was taken during the follicular phase (between the first and third days of the cycle), the second one in the ovulation period (between the 12th and 14th days), and the third one in the luteal phase (between the 23rd and 25th days). The following hormones were assessed: follicle stimulating hormone, luteinizing hormone, prolactin, 17- $\beta$ -estradiol, progesterone, dehydroepiandrosterone sulfate and testosterone. In men evaluation of the above-mentioned sex hormones was performed once. Eotaxin levels were measured in the same blood samples as the hormones. Enzyme-linked immunosorbent assay (R&D kits, Minneapolis, Minnesota, USA) was used to measure eotaxin levels and the electrochemiluminescence method (Roche Diagnostics, Mannheim, Germany) was used for sex hormones. Each sample was assayed twice and the mean of the 2 results was recorded. The *t* test was used to evaluate differences in

serum eotaxin concentration between males and females. The Pearson linear correlation coefficient (*r*) was calculated between hormones and eotaxin.

The mean (SD) age of subjects was 31 (8.4) years for women and 28 (7.3) years for men ( $P > .05$ ). The mean serum eotaxin level in women was significantly lower than in men: 132.5 (63.6) pg/mL in women vs 159.7 (88.7) pg/mL,  $P > .05$  in men. There was no correlation between serum eotaxin and sex hormone levels in women in consecutive phases of the menstrual cycle. Nor was there a correlation between serum eotaxin and follicle stimulating hormone, luteinizing hormone, prolactin, 17- $\beta$ -estradiol, progesterone and dehydroepiandrosterone sulfate hormone in males. However, a significant linear correlation was observed between the serum eotaxin and testosterone levels in men ( $r = 0.48$ ,  $P < .05$ ) (figure).



Correlation (Pearson coefficient, *r*) between serum eotaxin and testosterone levels in healthy men.

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### Food Allergy Due to Trout Roe

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Key words: Food allergy. Trout roe. Immunoblotting. Basophil activation test. Histamine release test.

Palabras clave: Alergia alimentaria. Huevas de trucha. Immunoblotting. Test de activación de basófilos. Test de liberación de histamina.

Roe allergy is a rare condition and few cases can be found in the literature [1,2], although some cases of allergy to trout roe have been reported [3]. We report the case of a patient allergic to trout roe.

A 28-year-old man with a history of allergic rhinitis caused by sensitization to mites presented with pharyngeal pruritus and bronchospasm, with associated dyspnea, immediately after consumption of trout roe. The dyspnea resolved spontaneously in 30 minutes. Twenty-four hours later, the patient presented similar symptoms, again after eating trout roe.

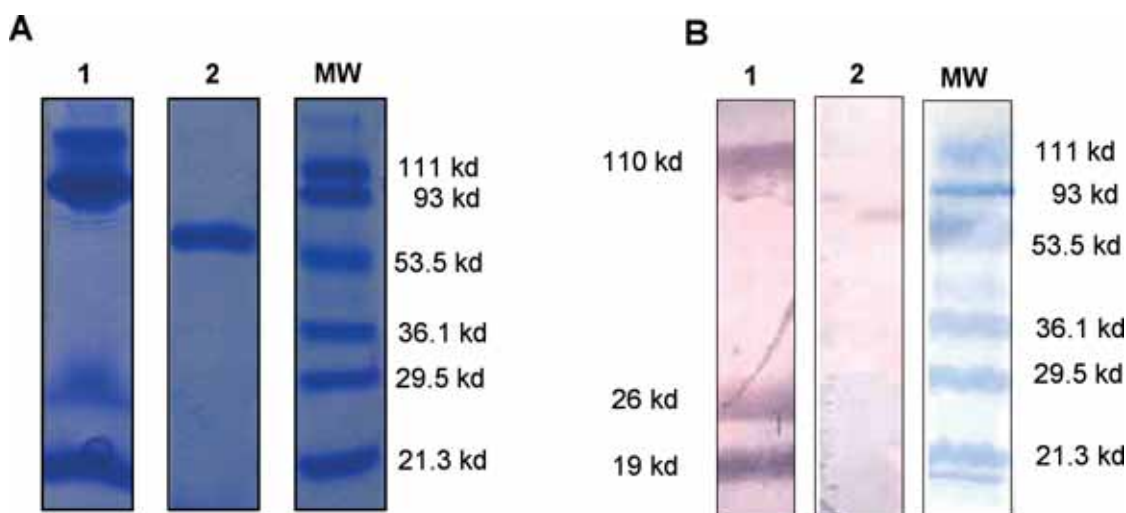
Skin tests with commercial extracts of mussel, clam, squid, prawn, crayfish, cod, sardine, megrim, hake, and trout were negative. Prick-by-prick test was positive with trout roe (10 × 12 mm papule) and negative to trout, salmon roe, and Beluga caviar.

In a single blind oral challenge test, the patient tolerated trout, salmon roe, and caviar. Trout roe was not tested due to the risk involved. The patient tolerated fish without problems.

Total serum immunoglobulin (Ig) E concentration was 65 kU/L and in analysis of serum specific IgE to cod, sardine, salmon, trout, and hake, all had concentrations below 0.35 kU/L.

Positive antigen-specific responses were observed in the histamine release test, basophil activation test, and sulfidoleukotriene release test with trout roe (10.2%, 70.4%, and 8344 pg/mL, respectively) but the results were negative with trout (0%, 0.7%, and 248 pg/mL, respectively). Two healthy control subjects had negative results in all the in vitro tests to the same extracts.

We performed sodium dodecyl sulfate polyacrylamide gel electrophoresis with trout roe and trout extracts (10%



A) Sodium dodecyl sulfate polyacrylamide gel electrophoresis with trout roe (lane 1) and trout (lane 2). B) Immunoblot with the patient's serum (lane 1, trout roe; lane 2, trout). MW indicates molecular weight marker; kd, kilodalton.

in phosphate buffered saline) and detected 4 bands ranging between 130 and 19 kilodaltons (kd) for trout roe and a single 70 kd band for trout. Immunoblotting with the patient's serum revealed the presence of IgE binding to 110, 26, and 19 kd bands only in the trout roe extract (figure).

We report a case of trout roe allergy confirmed by positive results in both in vivo and in vitro tests. The patient also tolerated trout and roe from other fish species, as in a previously described case [3]. Immunoblotting revealed 3 bands in trout roe extract that were recognized by specific IgE. The bands with the lowest molecular weight (19 and 26 kd) seem to correspond to those described by Makinen-Kiljunen et al [3]. The 110 kd band could correspond to vitellogenin or lipovetellin [4], proteins produced by the liver and present in the sexually mature female oocytes of oviparous and ovoviviparous animals and which have been described as allergens in the case of caviar allergy [2]. Nevertheless, as our patient did not present symptoms with other fish roe, we believe this band may correspond to a different protein.

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## Drug Rash With Eosinophilia and Systemic Symptoms After Ibuprofen Intake

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Key words: DRESS. Ibuprofen.

Palabras clave: Eritema medicamentoso con eosinofilia y síntomas sistémicos. Ibuprofeno.

Drug rash with eosinophilia and systemic symptoms (DRESS) is a syndrome of severe adverse drug reaction that occurs 1 to 8 weeks after initiating therapy with certain drugs [1]. The symptoms of DRESS represent internal organ injury with eosinophilia. Most often it starts with fever, skin rash and enlarged lymph nodes. These signs are followed by liver and renal impairment, pulmonary and cardiac infiltrates and hematological abnormalities, principally eosinophilia and lymphocytosis with large, atypical lymphocytes [1]. The majority of described DRESS cases are attributed to anticonvulsant drugs [1], but other drugs may also induce DRESS.

We report a rare case of DRESS after ibuprofen intake. A 23-year old man was started ibuprofen because of flu-like symptoms. He took only 1 tablet at midday. On the evening of the same day he noticed itching and a maculopapular rash on his forearms. During the next few days the rash spread over his upper limbs, neck, face, chest and feet. Subsequently facial edema appeared, mostly around his eyes. Five days after intake of a single dose of ibuprofen, yellowish skin discoloration and sclera, dark urine, and decoloration of feces became evident. The symptoms worsened and the patient was admitted to hospital. Laboratory tests showed liver failure (transaminases over 700 IU/L) with prolonged prothrombin time (16.93 seconds), cholestasis ( $\gamma$ -glutamyl transpeptidase, 325 U/L; alkaline phosphatase, 192 U/L; bilirubin, 3.91 mg/dL), and kidney failure with proteinuria and erythrocyturia. Eosinophilia was 5% (white blood cell count,  $10 \times 10^9/L$ ). No hepatotropic viral infection was evident (negative for hepatitis B antigen, hepatitis C virus [HCV] antibodies, HCV-RNA, and anti-hepatitis A virus immunoglobulin [Ig] M). Assays to detect antinuclear antibodies, antimitochondrial antibodies-2, and anti-cytomegalovirus (CMV) antibodies were also negative. Immediately after diagnosis corticosteroid therapy was started (dexamethasone 5 mg/day) and cutaneous symptoms soon disappeared and exfoliative dermatitis started on the patient's back and the palms of his hands. Liver and kidney functions improved slowly to resolution (liver enzymes were almost fully normalized). The dose of dexamethasone was reduced gradually and the patient was discharged from hospital. He declined skin tests with ibuprofen.

The pathogenesis of DRESS is not fully understood. It could originate from impaired liver metabolism of certain drugs

leading to the generation of reactive metabolites. Ibuprofen is extensively metabolized in the liver to pharmacologically inactive metabolites. It is mainly oxidized followed by acyl-glucuronidation. Liver metabolism involves cytochrome P450 isoenzymes CYP2C9 and CYP2C8 [2]. So far ibuprofen has been described as a poor immunogen that is metabolized without highly-reactive metabolites, and the case we report is one of the very rare ibuprofen induced DRESS reactions reported in the literature [3]. Individual variability in blood levels of ibuprofen may be caused by polymorphism of CYP isoenzymes.

DRESS may also be caused by cofactors such as acute viral infection. Recently the role of the Epstein-Barr virus, the CMV, and the human herpes virus-6 (HHV-6) in the pathogenesis of DRESS has been postulated. Our patient's CMV antibody assay was negative. As published recently by Descamps et al [4], DRESS could also be caused by reactivation of a latent HHV-6 virus infection. We did not test for either HHV-6 or Epstein-Barr virus infection, but it is worth mentioning that our patient started ibuprofen because of flu-like symptoms, and the coincidence of viral infection cannot be ruled out.

The question that should be addressed is the safe use of drugs in the future. In previously sensitized patients, DRESS may also be induced within 1 day upon rechallenge. Therefore patients who have experienced DRESS should be warned and the drug that provoked the reaction or drugs that share its chemical features must be avoided. Primary prevention of DRESS depends on appropriate initial dosing and appropriate dose escalation [1]. The activity of detoxifying enzymes responsible for drug metabolism is genetically regulated and family members should also be made aware of the incident. It may happen that another drug, not the culprit one, will induce DRESS in the future. The literature contains cases of second DRESS episodes induced by the drug used for treatment of the symptoms of first DRESS. Antibiotics and paracetamol are usually involved [5]. Further studies are warranted to find a diagnostic tool with good prediction properties to guide the introduction of new drugs for patients who have experienced DRESS.

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## Allergy to Basil, a Lamiaceae Herb

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Key words: Labiatae. Basil. Oregano. Lavender. Food allergy.

Palabras clave: Plantas labiadas. Albahaca. Orégano. Lavanda. Alergia alimentaria.

Basil (*Ocimum basilicum*) and oregano (*Origanum vulgare*) are food seasonings, eaten raw or cooked. They belong to the Lamiaceae (formerly Labiatae) plant family, which also includes thyme, hyssop, marjoram, mint, spearmint, rosemary, sage, pennyroyal, lavender, and others. Although they are widely used in the Mediterranean diet, only 1 case of food allergy to oregano and thyme has been reported [1]. We report the first 2 cases of allergy to basil.

A 65-year-old woman reported an episode of dyspnea, urticaria, and angioedema involving the face and lips occurring within 30 minutes of eating homemade pesto genovese sauce containing raw basil, pine nuts, garlic, olive oil, and parmesan cheese. She had experienced oral pruritus each time she tasted oregano in a salad containing tomato, cucumber, feta cheese, and olive oil. The same salad caused no problem to her when it did not contain oregano. She also gave a history consistent with the sudden onset of sneezing, nose congestion, coughing, and wheezing every time she smelled lavender.

A 25-year-old male complained of oral pruritus, rhinorrhea, nose congestion, eye pruritus, angioedema on his lower lip, and emesis occurring 15 minutes after eating pesto sauce made with the same recipe as above. He reported a 7-year history of seasonal rhinitis, conjunctivitis, and asthma and a history of systemic allergic reactions to pistachio and cashew nuts. He also complained of oropharyngeal pruritus every time he tasted walnuts.

Both patients reported that after the episode they continued to eat some ingredients of pesto sauce (garlic, olive oil, parmesan cheese and pine nuts), with no problem. They had never tasted basil since the episode.

Skin prick tests (SPT) with a panel of food and inhaled allergens (Alyostal Prick, Stallergenes, Antony Cedex, France) were performed. Patients were also tested using the prick to prick (P-P) technique with dried commercial Lamiaceae plants (basil, oregano, thyme, lavender, rosemary, marjoram, mint and sage) moistened in 0.9% normal saline as well as with

pine nuts, garlic, olive oil and parmesan cheese. Wheals with a diameter greater than 3 mm and flare diameter greater than 10 mm were considered positive. P-P to Lamiaceae herbs performed on 10 volunteers (5 healthy individuals and 5 non-food – allergic atopic patients) were negative, confirming the specificity of the P-P skin testing. Further studies included a blood count, total serum immunoglobulin (Ig) E and specific IgE assays (sIgE, ImmunoCAP, Pharmacia, Uppsala, Sweden) to Lamiaceae allergens (thyme, marjoram, and basil) and to the allergens for which positive SPT reactions were observed. IgE-immunoblotting was not available. A challenge test was proposed to both patients but they both declined.

Patient 1 had positive tests to *Artemisia vulgaris* and to all Labiatae tested. Patient 2 had positive tests to Gramineae species, basil, oregano, lavender, pistachio, cashew nut, hazelnut, almond, walnut and celery. The tests for sIgE to basil, marjoram, and thyme were negative in both patients. They were advised to completely avoid the ingestion of basil and an epinephrine autoinjector was prescribed to each.

IgE-mediated allergic reactions due to Lamiaceae are very rare [1-5]. In most reported cases of Lamiaceae allergy the performed in vitro tests were negative and the diagnosis was confirmed only by in vivo skin testing. Skin testing reveals cross-sensitivity among Lamiaceae plants, not always followed by clinical cross-reactivity [1,2]. Food allergy to Lamiaceae is observed in pollen-allergic patients, but each patient is sensitive to pollen of different families. Further studies have to be done to clarify the underlying cross-reacting mechanisms of the different Lamiaceae epitopes.

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