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NO in the pathogenesis of cell injury have yielded conflicting results. It is not yet clear whether NO produced in inflammatory states serves as a mediator of cell damage or as a defense mechanism under conditions of oxidant stress. It is well established that NO and O₂— can combine to form peroxynitrite, that itself is cytotoxic.¹ However, Chang et al⁷ have demonstrated in rats that NO protects against oxidant cytotoxicity in several cell types, including pulmonary endothelium. Therefore, it could be speculated that under conditions of increased oxidative stress, the inducible nitric oxide synthase enzyme activity could be upregulated by some proinflammatory cytokines, resulting in a protective mechanism on pulmonary cell damage. Some authors have also shown that exposure to some oxidants, such as NO₂, in healthy subjects could affect F_ENO levels, although supplementation with ascorbic acid does not affect these levels, suggesting that ascorbic acid has no significant effect on the NO metabolism of the epithelial lining fluid *in vivo*.⁸ Furthermore, Dunstan et al⁹ recently failed in showing a relationship between F_ENO and serum levels of some antioxidant vitamins in allergic adults.

A major limit of the present study was the fact that about 50% of our patients had received a short course of ICSs before the study. This could have contributed to reducing the degree of correlation observed in our population of patients, as F_ENO levels dramatically decrease with steroid therapy in most patients with asthma.⁵ Furthermore, it cannot be excluded that other confounding dietary or nondietary factors, not considered in the present analysis, could have played a role in the correlations observed. Food patterns, rather than specific foods, could theoretically have been responsible for the outcomes. The possibility of a “reverse bias,” ie, that children with a specific symptom or disease could have different dietary habits, should also be taken into consideration. Although our preliminary findings warrant confirmation by other groups and in healthy individuals on larger study populations, the data emerging from the present study suggest that F_ENO measurement could provide new insights into the relationship among food consumption, oxidative stress, and asthma.

We thank Dr Giuseppe Lippolis of Telenet Srl, Padova, Italy, for statistical support, and Dr Vito Paolo Logrillo of the Department of Pediatrics, Bari, Italy, for technical support.

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Supported by the University of Bari, Bari, Italy.

Disclosure of potential conflict of interest: The authors have declared that they have no conflict of interest.

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Available online March 6, 2007.
doi:10.1016/j.jaci.2007.01.028

Pathergy response to skin prick testing

To the Editor:

Delayed skin test reactions, both isolated and after an immediate reaction, have previously been reported more commonly after intradermal skin testing than skin prick testing.¹⁻³ After skin prick testing, our patient developed a pathergy response, a rare cutaneous erythematous and pustular reaction 24 hours after skin trauma that is associated with a vasculitic response histologically.

A 46-year-old woman presented to our clinic for evaluation of allergic rhinitis. She had classic nasal and ocular symptoms consistent with allergic rhinitis. Her symptoms were present perennially with seasonal exacerbations in the spring and fall. Five years before her presentation, she received immunotherapy for approximately 6 months, but she discontinued immunotherapy because of her schedule. She had no previous adverse reactions to skin testing, immunotherapy, or other skin trauma. She denied any arthralgias, gastrointestinal symptoms, mucosal ulcerations, cutaneous symptoms, or history thereof. Skin prick testing to 53 aeroallergens was performed using the QUINTEST (HollisterStier Laboratories, LLC, Spokane, Wash) device. Allergies to multiple trees, grasses, weeds, molds, and environmental were found. Five days after skin testing, she reported that she developed pustules at the skin testing sites 24 hours after the skin tests were applied. She also had complaints of intense local pruritus. Physical examination revealed discrete, uniform, round, erythematous patches ranging from 1.0 cm to 1.2 cm in diameter, over her back in the

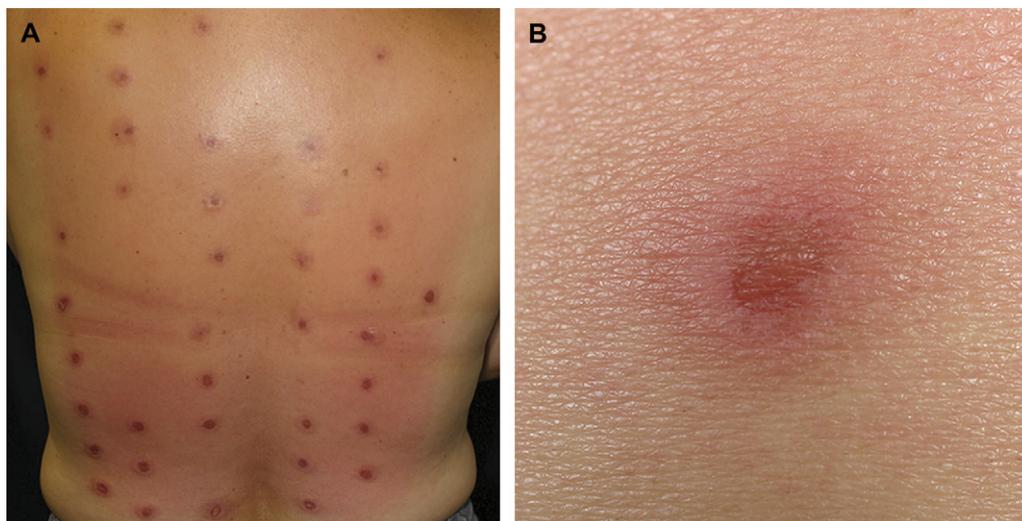


FIG 1. Pathergy response on the back in the pattern of skin prick testing (A) with close-up (B).

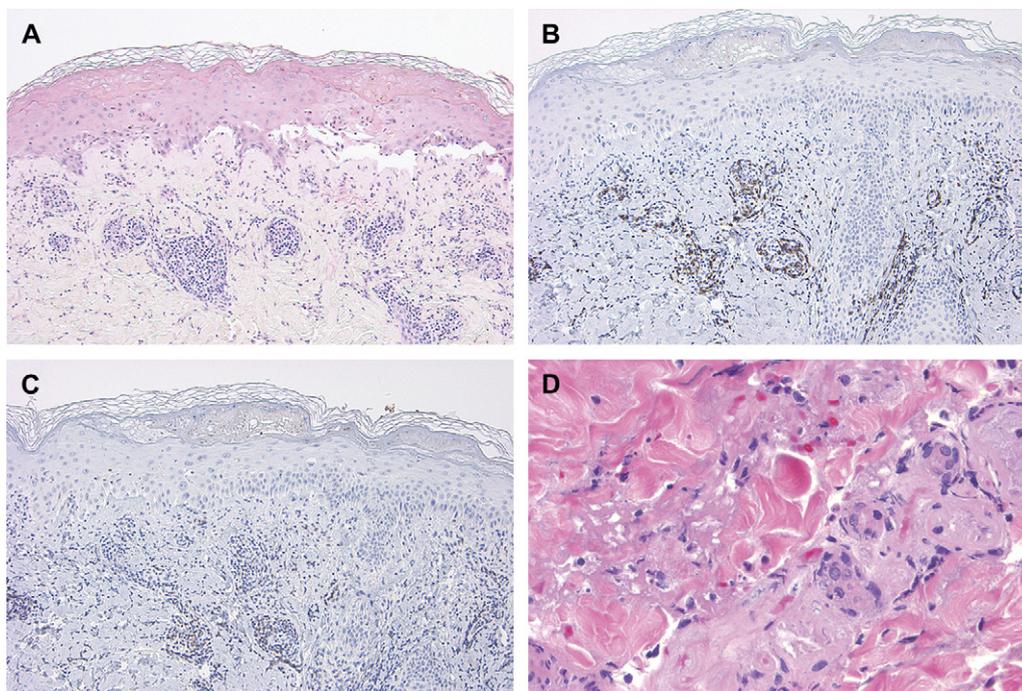


FIG 2. Punch biopsy of pathergy lesion at $\times 20$ magnification, stained with hematoxylin and eosin (A), CD8 immunostain (B), and CD4 immunostain (C). D, Punch biopsy 24 hours after intradermal injection of histamine into forearm, stained with hematoxylin and eosin, $\times 40$.

pattern of skin prick testing sites (Fig 1, A and B). Central brown macules, vesicles, erosions, and crusts were also observed within the erythematous patches. These reactions were present at 37 of 40 sites that had a 1+ or greater reaction, including the histamine control, but reactions were present in only 2 of 15 sites that lacked reactivity at the time of initial reading. Histopathologic examination of a reaction site punch biopsy demonstrated abundant

necrotic keratinocytes, extensive interface vacuolar changes, focal subepidermal vesicle formation, and superficial perivascular lymphocytic infiltrates (Fig 2, A). Immunostaining for lymphocyte markers demonstrated almost 100% of the lymphocytes were T cells (CD3 staining) with few to no B cells (CD20); most T cells were stained with CD8 (Fig 2, B) rather than CD4 (Fig 2, C). Laboratory results revealed normal complete blood count,

antinuclear antibodies, rheumatoid factor, and C-reactive protein.

As it was thought that our patient had experienced a pathergy reaction, additional pathergy testing was performed so that a biopsy could be obtained after 24 hours rather than 5 days. We performed a histamine trap test by intradermally injecting 0.05 mL of 1-mg/mL histamine solution into the volar surface of the right forearm, per the protocol outlined by Jorizzo et al⁴ in their study of histologic changes in pathergy reactions. After 24 hours, an erythematous macule was present at the site of injection and a punch biopsy was obtained after infiltration of 1% lidocaine without epinephrine. Histopathologic examination revealed superficial and deep perivascular mixed dermal infiltrate of neutrophils and lymphocytes, endothelial swelling of blood vessel walls, perivascular accumulation of neutrophils, and minor focal leukocytoclasia and hyaline deposition (Fig 2, D). Immunostaining for lymphocyte markers was again performed, and the lymphocytes present were almost all T cells, but no appreciable difference was found in the weak staining for CD4 and CD8. These clinical and histologic findings are consistent with the pathergy response observed in patients with Behçet's disease, the prototypical disease that exhibits pathergy.⁴

Although previous skin test results were available, records of the patient's past immunotherapy prescription could not be obtained. No correlation was found between previous skin prick test results and allergen sites that subsequently developed a pathergy response; pathergy reactions sites were evenly split between 18 allergens that had been previously positive on skin prick testing and 20 allergens that had been previously negative on skin prick testing. Presumably only allergens that gave positive responses on previous skin prick testing would have been used for immunotherapy. Thus, we do not believe the pathergy reaction of this patient was a response to previous immunotherapy.

Pathergy has been associated with several disease entities, including Behçet's disease, pyoderma gangrenosum, eosinophilic pustular folliculitis, cutaneous ulcerative lichen planus, bowel-associated dermatosis-arthritis syndrome, rheumatoid arthritis, leukocytoclastic vasculitis, non-hodgkin lymphoma, and chronic myeloid leukemia treated with interferon- α .^{4,9} Jorizzo et al⁴ proposed that the pathergy response in Behçet's disease may be explained by a combination of circulating immune complexes, perhaps from associated diseases, and an unknown factor in the serum that enhances neutrophil migration. A previous report showed no pathergy response after skin prick testing to common aeroallergens in a collection of 30 patients with Behçet's disease, despite many of them having a positive pathergy test.⁵ Physicians conducting skin prick testing should be aware of pathergy as a rare adverse event and consider associated diseases in patients in whom this reaction occurs. Given the uncertain etiology of the development of a pathergy response in this patient, immunotherapy was not offered as a treatment option. Our patient may over time develop symptoms consistent with a known pathergy-

associated illnesses, which may explain why she developed this response after skin prick testing.

We thank our dermatopathologists, Lt Col (Dr) Michael R. Murchland and Lt Col (Dr) Marcus S. Fisher, for their assistance.

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Disclosure of potential conflict of interest: M. Rathkopf has received grant support from Novartis and ZLB Behring; is employed by Allergy, Asthma, and Immunology Center of Alaska, LLC; and is on the speakers' bureau for Genentech. The rest of the authors have declared that they have no conflict of interest.

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Available online March 15, 2007.
doi:10.1016/j.jaci.2007.01.033

The predictive relationship of food-specific serum IgE concentrations to challenge outcomes for egg and milk varies by patient age

To the Editor:

It is complicated to interpret food-allergy symptoms in children because of the dynamic nature of the allergic response that changes with time: the acquisition of food tolerance and amelioration of symptoms is reported in children with all types of food allergy.¹ The various diagnostic errors and pitfalls in the management of food allergy suggest that we should utilize all available tests more fully in the best interests of the patient. Sampson