

was suspected, this must have been evenly distributed in both diet subgroups. We attribute the positive clinical differences to milk allergy. Children at risk for milk allergy constituted the "control group."

The speculation of Cantani et al about the concentration of CB IgE in the II-IV groups is not accurate; patients with CB-IgE were equally distributed in all subgroups.

R. WILLEMS
G. CASIMIR
Brussels, Belgium

REFERENCES

1. Bahna S, Heiner D. Allergies to milk. New York: Grune and Stratton, 1980.
2. Bahna S. The diagnostic dilemma of milk allergy. *Ann Allergy*. 1989;63:475-6.

ASPIRIN INTOLERANCE

To the Editor:

We have several concerns about the recent article by Dr. Andri, et al.¹ First, we are concerned about the use of the phrases "aspirin intolerance" and "aspirin sensitivity." Despite the "aspirin-sensitive" title, the authors state, "The clinical symptoms of ASA-intolerance are bronchial asthma and/or rhinitis, urticaria/angioedema, and anaphylactoid shock," in the paper. They are describing 3 types of aspirin sensitivity, not aspirin intolerance. Aspirin intolerance is less specific, and in our view, would properly describe the gastrointestinal distress caused by aspirin.

Individuals with respiratory aspirin sensitivity (aspirin-sensitive asthma) have underlying chronic rhinitis, sinusitis, nasal polyps and asthma and develop acute inflammation of the respiratory tract after ingestion of aspirin. Cutaneous aspirin sensitivity refers to flares of urticaria and/or angioedema after ingestion of aspirin, generally in patients with chronic idiopathic urticaria and angioedema. The third group of aspirin sensitive patients develop anaphylactoid (non-IgE mediated) reactions. Although all of these "aspirin

sensitive" patients react after taking aspirin and all cross-reacting substances, the pathophysiology, prognosis and treatment of these three currently recognized groups are different. A separate group of patients develop IgE-mediated anaphylaxis to a specific nonsteroidal anti-inflammatory drug, and do not cross-react with others, or with aspirin.^{2,3}

Since all these groups, and maybe more as yet unrecognized, were represented among the 429 subjects studied, and only 22% of the subjects had asthma as the "documented intolerance," and none of the reactions to nimesulide were bronchospasm, we are not sure what this paper means for our aspirin-sensitive asthmatic patients.

BERNARD A. FEIGENBAUM, MD
RONALD A. SIMON, MD
DONALD D. STEVENSON, MD
Scripps Clinic and Research
Foundation
La Jolla, California

REFERENCES

1. Andri L, Senna G, Betteli C, et al. Tolerability of nimesulide in aspirin-sensitive patients. *Ann Allergy* 1994; 72:29-32.
2. Manning ME, Stevenson DD, Mathison DA. Reactions to aspirin and other nonsteroidal anti-inflammatory drugs. *Immunol Allergy Clin NA* 1992;12: 611-31.
3. Stevenson DD, Simon RA. Sensitivity to aspirin and nonsteroidal antiinflammatory drugs. In: Middleton E, ed. *Allergy principles and practice*, 4th ed. St. Louis: Mosby, 1993;1747-65.

Response:

"Aspirin intolerance," is often used as a synonym for "aspirin sensitivity."¹⁻⁶

The main problem of aspirin-sensitive patients is the availability of a safe anti-inflammatory drug to be taken when needed. Our results showed that nimesulide is a safe drug in a very large group of patients. In this study 94 patients were affected by documented asthma after ingestion of aspirin. The challenge test with nimesulide was negative in all the subjects. We agree

that some patients have asthma after the administration of one NSAID and not after another. In order to study the pathogenesis of the aspirin sensitivity in these patients it is mandatory to perform challenges with aspirin and other NSAIDs. However the Consensus Report of the Italian Society of Allergy and Immunology on "Diagnosis of Drug Allergy" stated that the skin test with aspirin is not indicated in aspirin sensitive patients and the challenge test is allowed only for an alternative drug, but not for drugs known to provoke possible acute asthma in these patients.⁷ Further, in our opinion, a challenge with aspirin or other NSAIDs is unethical in patients with high probability of dangerous reactions after the challenge.

The aim of our study was to determine whether a drug like acetaminophen can be administered safely to a large group of aspirin sensitive patients. The very low frequency of reactions to nimesulide in our study supports the safety of this drug. The IgE-mediated mechanism in aspirin sensitivity is only hypothesized lacking demonstration of aspirin-specific IgE. An IgE-mediated mechanism is only suggested for NSAID-induced hypersensitivity pneumonitis.⁸ Further, although others have suggested an IgE-specific pathogenesis, the results are controversial since one study showed aspirin-IgE-specific antibodies in ASA-induced urticaria,⁹ whereas another failed to find these antibodies.¹⁰ Other studies performed by De Weck and Schwartz showed that impurities in commercial acetylsalicylic acid like acetylsalicylic anhydride, acetylsalicylsalicylic acid can evoke the IgE-specific antibodies.¹¹ These results, however, have never been confirmed in following studies. The IgE-specific mechanism in aspirin sensitive asthma is still very controversial.

LUIGI ANDRI, MD
Servizio Autonomo di Allergologia
Istituti Ospitalieri di Verona
Verona
Italy

REFERENCES

1. Samter M, Beers RF. Intolerance to aspirin. *Ann Intern Med* 1968;68:957-83.
2. Malmgren R, Unge G, Zetterstrom O, et al. Lowered glutathione-peroxidase in asthmatic patients with food and aspirin intolerance. *Allergy* 1986;41:43-5.
3. Goetzel EJ, Valacer DJ, Payan DG, Wong MYS. Abnormal responses to aspirin of leukocyte oxygenation of arachidonic acid in adults with aspirin intolerance. *J Allergy Clin Immunol* 1986;77:693-8.
4. Picado C, Carillo JA, Schinca N, et al. Effects of fish oil enriched diet on aspirin-intolerant asthmatic patients: a pilot study. *Thorax* 1988;43:93-7.
5. Nizankowska E, Szczeklik A. Glucocorticosteroids attenuate aspirin-precipitated adverse reactions in aspirin-intolerant patients with asthma. *Ann Allergy* 1989;63:159-62.
6. Nizankowska E, Dworski R, Soja J, Szczeklik A. Salicylate pretreatment attenuates intensity of bronchial and nasal symptoms precipitated by aspirin in aspirin-intolerant patients. *Clin Exp Allergy* 1990;20:647-52.
7. SIAIC. Diagnostica di allergia a farmaci. Memorandum della Società Italiana di Allergologia e Immunologia Clinica. *Folia Allergol et Immunol Clin* 1989;36:437-65.
8. Stevenson DD, Simon RA. Sensitivity to aspirin and nonsteroidal anti-inflammatory drugs. In Middleton E, ed. *Allergy principles and practice*, 4th ed. St. Louis: Mosby, 1993:1759.
9. Phillips JA, Perelmutter L. IgE-mediated and non IgE-mediated allergic-type reactions to aspirin. *Acta Allergologica* 1974;29:474-90.
10. Krilis S, Gregson RP, Basten A, Ballo BA. Investigation of the possible involvement of IgE anti-salicyloyl antibodies in patients with urticaria. *Int Arch Allergy Appl Immunol* 1981;64:293-301.
11. Bundgaard H, De Weck AL. The role of amino-reactive impurities in acetylsalicylic acid. *Int Arch Allergy Appl Immunol* 1975;49:119-24.