

# Sensitivity to non-acetylated salicylates in a patient with asthma, nasal polyps, and rheumatoid arthritis

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*A woman experienced exacerbations of bronchial asthma after taking aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) for rheumatoid arthritis. On oral challenges, she developed an urticarial reaction after tartrazine; urticarial and bronchospastic reactions after salicylsalicylic acid; and urticarial and bronchospastic reactions after choline magnesium trisalicylate. Non-acetylated salicylates have been recommended for use in aspirin- and/or tartrazine-sensitive patients. The results of sensitivity studies of our patient indicates that such patients may also be sensitive to non-acetylated salicylates.*

## ABBREVIATIONS

MMEF,	maximal mid-expiratory flow rate
NSAIDs,	non-steroidal anti-inflammatory drugs
PF,	peak expiratory flow
PFT,	pulmonary function tests

## INTRODUCTION

Sensitivity to aspirin and other NSAIDs has been reported in asthmatic and other patients.<sup>1-7</sup> Patients' symptoms are usually bronchospastic, urticarial, or both.<sup>4</sup> It has generally been accepted that non-acetylated salicylates, such as choline salicylate or salicylsalicylic acid, are tolerated by these patients.<sup>1,3,5</sup> We describe a patient with asthma, nasal polyps, and rheumatoid arthritis who developed bronchospastic and urticarial reactions after administration of choline magnesium trisalicylate and salicylsalicylic acid, as well as multiple other NSAIDs and tartrazine.

## CASE REPORT

The patient is a 49-year-old white female with a history of mild, intermittent asthma since age 21 years. When she was 46 years old, she developed seropositive rheumatoid

arthritis. She had exacerbations of her asthma after taking aspirin for joint pain. She was then treated with naproxen (Naprosyn) 500 mg B.I.D. and developed status asthmaticus. Subsequently, she received a variety of NSAIDs, including tolmetin sodium (Tolectin), sulindac (Clinoril), ibuprofen (Motrin), piroxicam (Feldene), diflunisal (Dolobid), phenylbutazone (Butazolidin), and benoxoprofen (Oraflex) with varying effects on her arthritis. Her asthma continued to worsen.

The patient was first seen by us in March, 1983 at which time she was found on physical examination to have nasal polyps and wheezing. A diagnosis of triad asthma (Samter's syndrome) was made on the basis of her asthma, nasal polyps, and history of aspirin sensitivity. Choline magnesium trisalicylate (Trilisate) was recommended, but her asthma continued to be symptomatic while taking the non-acetylated salicylate despite treatment with theophylline and albuterol.

In April, 1984, the patient was re-evaluated. Positive findings on physical examination included a nasal polyp on the left side, bilateral inspiratory and expiratory wheezes, and joint findings consistent with rheumatoid arthritis. Laboratory studies included hemoglobin = 11.7 g/dL; white blood cell count = 11,400 per mm<sup>3</sup> with 36% neutro-

phils, 9% band forms, 27% lymphocytes, 2% monocytes, and 24% eosinophils; Westergren sedimentation rate = 54 mm/h; positive rheumatoid factor; negative antinuclear antibody; and positive radioallergosorbent tests (RAST) for house dust, animal dander, grass pollens, and molds. On prick skin testing she exhibited significant dermographism. A chest x-ray was normal. Pulmonary function testing revealed a MMEF of 54% predicted and FEV<sub>1</sub>/FVC of 76% predicted, consistent with mild obstruction.

## METHODS

After informed consent was obtained, single-blind oral challenges with tartrazine, salicylsalicylic acid (Disalcid), and choline magnesium trisalicylate (Trilisate) were performed on different days. Increasing oral doses of each agent were administered hourly. Baseline PFTs were performed and repeated every 30 minutes. The challenge was considered positive if urticaria or angioedema developed, or if a 15% or greater drop in PF was measured.

## RESULTS

### *Tartrazine*

The patient was given 1 mg of tartrazine orally. Urticaria developed over her face and neck with mild angioedema within 30 minutes. No further doses of tartrazine were ad-

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ministered. Over the next hour there were no significant changes in PFT values.

#### *Salicylsalicylic Acid*

The patient received 50 mg of salicylsalicylic acid (Disalacid) orally. Within 60 minutes urticaria developed over her neck, abdomen, and feet. At the same time, the patient complained of chest tightness and a 17% decrease in PF (from 84% predicted to 67%) was measured.

#### *Choline Salicylate*

Urticaria and mild angioedema developed 30 minutes after receiving 100 mg of magnesium choline trisalicylate (Trilisate). Wheezing was noted and, an additional 30 minutes later, a 25% decrease in PF (from 74% predicted to 49%) was seen. The bronchospasm was eventually reversed by inhaled albuterol. An earlier 50 mg dose had not provoked a reaction.

### DISCUSSION

Aspirin sensitivity is well recognized in patients with chronic urticaria, asthma, nasal polyps, or rhinosinusitis.<sup>1-7</sup> Settupane has reported that aspirin intolerance occurs most commonly in patients with chronic urticaria (23% to 28%) where an urticarial response is seen and in patients with asthma (4% to 19%)

who develop bronchospastic reactions.<sup>4</sup> He also states that the frequency of aspirin intolerance in patients with nasal polyps is 14% to 23% and the response is generally bronchospastic.

Cross-reactivity between aspirin and tartrazine in aspirin-sensitive patients has been described.<sup>1-4</sup> In double-blind studies, the frequency of aspirin-sensitive patients who react to tartrazine is between 8% to 15%.<sup>4</sup> The symptoms produced by tartrazine are similar to those produced by aspirin in such patients.

Cross-reactivity between aspirin and NSAIDs has been widely reported. The frequency of reactions to NSAIDs in known aspirin-sensitive patients has varied in different studies and with different agents from 20% to 100%. The use of non-acetylated salicylates has been suggested for therapy in patients who are aspirin and/or tartrazine sensitive<sup>1,3,5</sup>; however, the patient described here developed urticarial and bronchospastic reactions on oral challenge with choline magnesium trisalicylate and salicylsalicylic acid, two commonly used alternatives to NSAID.

The etiology of chemical sensitivities such as those to aspirin, NSAIDs, and tartrazine is unknown.<sup>1,3-6</sup> The experience with our

patient emphasizes that caution should be used in the routine substitution of non-acetylated salicylates in aspirin-sensitive patients.

### REFERENCES

1. Samter M, Beers FR: Concerning the nature of intolerance to aspirin. *J Allergy* 1967;40:218-293.
2. Juhlin L, Michaelsson G, Zetterstrom O: Urticaria and asthma induced by food-and-drug additives in patients with aspirin hypersensitivity. *J Allergy Clin Immunol* 1972;50:92-98.
3. Samter M: Intolerance to aspirin. *Hosp Prac* 1973;8:85-90.
4. Settupane GA: Aspirin and allergic diseases: a review. *Am J Med* 1983;74:102-9.
5. Mathison DA, Stevenson DD: Aspirin sensitivity in rhinosinusitis and asthma. *Immunol Allergy Prac* 1983;5:340-349.
6. Chiu JT: Aspirin-sensitive asthma. *Immunol Allergy Prac* 1983;389-392.
7. Lumry WR, Curd JG, Stevenson DD: Aspirin-sensitive asthma and rhinosinusitis: current concepts and recent advances. *Ear Nose Throat J* 1984;63:103-111.

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"Observation more than books, experience rather than persons are the prime educators."

A. Bronson Alcott