

### Immediate sensitization to methamizole verified by patch tests

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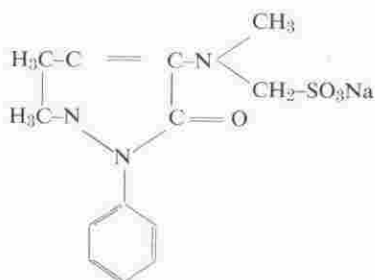
A 27-year-old nurse came to us because of itching and the appearance of wheals on her forearms when she prepared injections containing analgesics (unspecified). In the past, from the age of 12 until her first pregnancy at age 23, she had taken analgesics containing phenazonic compounds regularly during her periods. At age 26 she took an unspecified analgesic for back pain and had an immediate reaction of diffuse itching. Approximately 1 year later a tablet of Nisidina® produced anaphylactic shock.

Nisidina is a mixture of two antispastic drugs, adiphedrine and ethyl-N-diphenylaminoacetate, an antihistamine, diphenhydramine, and the analgesic methamizole (4-methylamino-1,5-dimethyl-2-phenyl-3-pyrazolone sodium methanesulfonate) which is sold in Italy under the name Novalgina®.

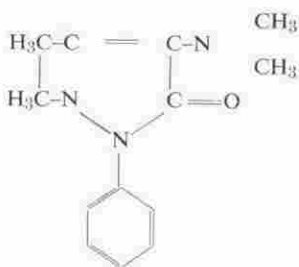
Patch tests with 10 % aminophenazone gave negative immediate and delayed reactions. The prick test with aminophenazone (10 %) and an intradermal test with a 1 % concentration both provoked an immediate wheal reaction.

A patch test with Nisidina (saturated solution) also provoked an immediate wheal reaction, but patch tests with the individual ingredients (10 % pet.) were all negative except for methamizole which gave an immediate wheal reaction. Prick tests with methamizole in concentrations of 1, 5, 25, and 50 % all provoked immediate reactions.

The structural formulas of methamizole and aminophenazone are:



Methamizole  
(Novalgina®)



Aminophenazone  
(Pyramidon®)

The results in this case support the use of patch tests in establishing an etiopathogenetic diagnosis in immediate allergic reactions. In addition, we have demonstrated the possibility of cross-reactions between methamizole and the commonly used aminophenazone (or Pyramidon).

### Anaphylactic shock from mustard after ingestion of pizza

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A young male patient came to our attention following hospitalization twice in 1 year for attacks of acute giant urticaria with edema of the

glottis which appeared while he was eating pizza margherita.

Intradermal tests with animal and vegetable

food allergens (Lofarma) all gave negative results except for the Brassicaceae group (turnip, cabbage, cauliflower, mustard plant) which provoked an intense wheal reaction. A daring intradermal injection of mustard antigen (extracted from seeds of both black and white mustard) caused an intense wheal reaction followed by shock and glottic edema, which resolved quickly with medical treatment.

The patient's sensitivity (PRIST:352 I.U.) to both white and black mustard seed was then controlled by radioallergosorbent test (RAST), using cellulose discs activated with CN Br and sensitized with 0.1 cc of extract obtained from the seeds of black and white mustard, and by reciprocal RAST inhibition tests.

| Substance                               | Net bound radioactivity of    |               |
|-----------------------------------------|-------------------------------|---------------|
|                                         | patient's serum               | control serum |
| <i>Brassica nigra</i>                   | 30.1 %                        | 0.6 %         |
| <i>Brassica alba</i>                    | 40.8 %                        | 0.4 %         |
| Pre-incubation of patient's serum with: | Net bound radioactivity of    |               |
| <i>Brassica alba</i>                    | <i>Brassica nigra</i> : 4.5 % |               |
| <i>Brassica nigra</i>                   | <i>Brassica alba</i> : 2.9 %  |               |

Extract of black mustard seed (chosen because it is more stable than white mustard) was filtered on a column of Bio Gel A 0.5 mm using an elution of phosphate tampon (PBS) 0.15M, pH 7.2. We obtained three fractions with positive direct RAST. The first and third were proteins, the other presented a profile which was not parallel to a protein optic density (280 nm). Thus black mustard contains at least three fractions with antigenic activity.

Since mustard seed is contained principally in prepared mustards, and not in pizza, we did patch tests with the mustards regularly used in the two restaurants.

| Brand             | Immediate reaction<br>(wheal 10'-20')         | Delayed reaction<br>(papulo-vesicular)<br>(48-72 h) |
|-------------------|-----------------------------------------------|-----------------------------------------------------|
|                   |                                               |                                                     |
| Amora of Dijon®   | +++                                           | +++                                                 |
| Bocquet of Dijon® | +++<br>(also diffuse itching, dyspnea, fever) | +++                                                 |

The ingredients of the two brands of mustard were the same: salt, vinegar, mustard seed, and the additives E330 (pectin) and E224 (sodium metabisulphite). All the results of patch and provocation tests done with the additives were negative.

Since 1) the patient was proven allergic to mustard, due to the ingredient mustard seed; 2) neither prepared mustard nor mustard seed nor powder, is used in pizza in general, and certainly not pizza margherita which is the simplest (flour, water, yeast, canned tomatoes, mozzarella cheese and olive oil); 3) the patient had eaten pizza in other restaurants in the same 12-month period with no adverse effects; and 4) prepared mustards are used regularly in pizza restaurants in other dishes, such as hot dogs; we think that our patient's acute allergic reactions were caused by ingestion of small amounts of mustard which had contaminated his pizza.

This case is presented, however, also because it shows the importance of patch tests in cases of IgE pathology with high sensitivity and the possible evolution of immediate reactions into delayed ones of still unknown mechanism.

#### Acknowledgments

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