

Measles and atopy – rash on rash?

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Key words: atopy; measles; positive association; rash.

● RECENTLY, Paunio et al. reported that atopic diseases occur more frequently in children and adolescents with a history of measles infection (1). Certain methodological problems were discussed in an accompanying editorial (2). More recently, Remes et al. have suggested that differential misclassification could explain the findings (3). In our opinion, the internal structure of the Finnish data supports this latter viewpoint. The 23 785 6-year-old children enrolled in November–December 1982, the first two months of the MMR vaccination project, had significantly lower atopic disease

prevalence ratios of measles cases to noncases than the remaining 102 518 6-year-old children recruited between January 1983 and June 1986 (Table 1). Since measles incidence decreased after the initiation of the MMR program with coverage reaching 97% (1), misclassified measles cases would tend to

We question an association between measles and atopic disease.

become an increasing proportion of self-reported measles cases after 1983, as speculated elsewhere by the authors (4). If the prevalence ratio of measles cases to noncases increases as the relative proportion of misclassified cases increases, this would suggest that misclassification may be a major reason for the reported positive association between measles and atopic disease.

Differences in vaccination coverage among allergic and nonallergic children could also have biased the association between measles and atopic diseases. Measles vaccination with monovalent measles vaccine was initiated in 1975, 7 years before the MMR project, but only with a coverage of 60–70% (1). As stated previously by the same group, “the term allergy is often not fully understood by the parents – or the physicians. . . . As a consequence, a considerable number of children remain inappropriately unvaccinated” (5). Fear of adverse reactions may very likely have prevented or delayed vaccination of atopic children. Surprisingly, Paunio et al. (1) report no data on vaccination coverage for monovalent measles vaccine among children with and without atopic diseases. Even small differences in vaccination coverage could produce large differences in the association between measles and atopic diseases.

Paunio et al. do not explain why they found a significantly positive association between measles infection and atopic

diseases. There is no information about the temporal relationship between measles infection and atopic diseases in the Finnish data. Two-thirds of the atopic children in the present study suffered from eczema. As eczema typically becomes manifest in early childhood, a large proportion of the atopic diseases must have occurred prior to measles infection.

In conclusion, the Finnish study provides no reason to believe that there is a positive association between measles infection and atopic diseases.

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References

1. PAUNIO M, HEINONEN OP, VIRTANEN M, LEINIKKI P, PATJA A, PELTOLA H. Measles history and atopic diseases: a population-based cross-sectional study. *JAMA* 2000; **283**:343–346.
2. GERN JE, WEISS ST. Protection against atopic diseases by measles – a rash conclusion? *JAMA* 2000;**283**:394–395.
3. REMES S, MAKELA M, MARSHALL J. Measles and atopy in Finland. *Allergy* 2000;**55**:973–974.

Table 1. Six-year-old children vaccinated in MMR vaccination program according to time of enrollment

	Eczema			Asthma			Rhinitis		
	Measles cases	Non-cases	Prevalence ratio§	Measles cases	Non-cases	Prevalence ratio§	Measles cases	Non-cases	Prevalence ratio§
Enrolled November and December 1982	200/1370	3044/22 415	1.07 (0.94–1.23)	62/1370	744/22 415	1.36 (1.06–1.76)	113/1370	1548/22 415	1.19 (0.99–1.43)
Enrolled January 1983 to June 1986	761/5414	9827/97 104	1.39 (1.30–1.49)	223/5414	2283/97 104	1.75 (1.53–2.00)	349/5414	4563/97 104	1.37 (1.23–1.52)
RR first/rest (95% CI)			0.77 (0.66–0.89)			0.78 (0.58–1.03)			0.87 (0.70–1.07)

Data for first period are based on data presented in Table 4 of original paper. Data for last period were provided by author.
§Measles cases vs noncases.

4. PELTOLA H, KARANKO V, KURKI T, et al. Rapid effect on endemic measles, mumps, and rubella of nationwide vaccination programme in Finland. *Lancet* 1986;1:137-139.
5. JUNTUNEN-BACKMAN K, PELTOLA H, BACKMAN A, SALO OP. Safe immunization of allergic children against measles, mumps, and rubella. *Am J Dis Child* 1987;141: 1103-1105.

Allergy to calcitonin

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Key words: calcitonin; cross-reactivity; desensitization; eel; human; rhinitis; salmon; urticaria.

● CALCITONIN is a polypeptidic hormone that regulates calcium metabolism. It is mainly used in severe osteoporosis treatment.

A 65-year-old woman reported eye and nose congestion, itching nose, and sneezing minutes after application of a salmon calcitonin nasal spray. She had tolerated this calcitonin previously. Her doctor modified the treatment to

daily parenteral administration.

Minutes after

the first dose of intramuscular (IM) salmon calcitonin, she developed an itching nose and generalized urticaria that wore off after parenteral administration of antihistamines and corticosteroids. After a second dose, she reported the same but milder symptoms, and she tolerated the third dose. She was able to finish the 15-day treatment cycle without further reactions.

Rhinitis and urticaria to salmon calcitonin.

The patient ate salmon and other fish without problems.

Skin prick tests with commercial salmon extract and salmon calcitonin (100 UI/ml) were negative. Skin prick tests with eel calcitonin (100 UI/ml) and the ID test with salmon calcitonin (1 UI/ml) were positive (both negative in 10 healthy control subjects). Skin prick (100 UI/ml) and ID tests with human calcitonin (1 UI/ml) were negative. We did not detect specific IgE antibodies to any calcitonin by the ELISA technique.

The patient was diagnosed as having salmon calcitonin allergy. Because of the molecular differences and the negative skin tests to the human product, the patient, after giving informed consent, underwent a simple blind controlled IM challenge with human calcitonin with good tolerance. She could follow the subsequent calcitonin cycles without further reactions.

Every calcitonin has 32 amino acids. All the calcitonins have a similar structure at both chain terminals. The amino acids in positions 1, 3, 4, 5, 6, 7, 9, 28, and 32 are the same in all calcitonins, while the amino acids in other positions vary among different species. Despite the phylogenetic factor, calcitonins are not more similar among mammals than between them and other animal groups.

Calcitonins can be classified by their structure into three groups:

- 1) pig, cow, and sheep (28 identical amino acids)
- 2) rat and human (30 equal amino acids)
- 3) salmon and eel (29 identical amino acids) (4).

The more common calcitonin side-effects are flushing, nausea, vomiting, and tingling hands. These reactions improve, in most patients, with continued therapy (1).

The positive skin tests in our patient and the negative results in 10 healthy controls strongly suggest the specificity of these tests.

Repetitive injections made the patient tolerant to salmon calcitonin, probably through a desensitization mechanism. During the refractory period of allergic reactions, patients may tolerate allergen re-exposure. Allergic reactions to calcitonin are rare and are usually referred to nonhuman calcitonins (2). However, adverse effects are more frequent and severe with the human species. Subcutaneous administration is safer than IM injections (1, 3).

Our skin tests suggest the existence of cross-reactivity between salmon and eel calcitonin, but not with the human one, probably because salmon and eel calcitonins are very similar. These two calcitonins differ in only three amino acids, while they both differ in 16 amino acids from the human one.

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References

1. MARTINDALE. The extra pharmacopoeia. 31st ed. London: Royal Pharmaceutical Society, 1996:776-777.
2. STUMPF JL. Pharmacologic management of Paget's disease. *Clin Pharm* 1989;8:485-495.
3. GENNARI C, PASSERI M, CHIERICHETTI SM, et al. Side-effects of synthetic salmon and human calcitonin [Letter]. *Lancet* 1983;1: 594-595.
4. AZRIA M. Las calcitoninas: Introducción. In: PITZER R, KÁLIN HB, editors. The calcitonins: physiology and pharmacology. Basel: Karger, 1989:1-19.