

The Aluminum Content in Some Patch Test Allergens

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ABSTRACT

The Al content of 18 patch test allergens were measured by electrothermal atomic absorption spectrophotometry. It was found that these preparations contained Al in various amounts. We conclude that the presence of Al in patch test allergens may interfere with the diagnosis and evaluations of patients to whom the test is applied.

Index Entries: Al; patch test allergens; atomic absorption spectrometry, microwave digestion unit.

INTRODUCTION

Aluminum (Al) is an abundant element, comprising approximately 8% of the earth's crust. However, because of its position in the periodic table and its abundance in the solar system, it has been suggested that Al is an essential element; there is no conclusive evidence that Al is an essential element in animals and humans (1-4).

There is no established biologic requirement for Al in human beings, but there are toxic effects associated with Al accumulation in tissues such as brain or bone. There is a lot of evidence that Al can accumulate in patients, especially in newborns, with reduced renal function owing to impaired excretion of Al. Al is also important because of its role in the

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etiology of such disorders as dialysis encephalopathy, osteomalacia, microcytic hyochromic anemia, and Alzheimer's disease (1,5,6). It has also been suggested that Al is a neurotoxin, membrane toxin, and an environmental toxin. Because of its wide use in industry and medicine, this is an element to which humans are highly exposed. Large amounts of Al are able to enter orally and through other routes (1,2,7).

Al compounds are used extensively in cosmetics and medicinal preparations in which advantage is taken of their astringent, antacid, antibacterial, and antiperspirant properties. Additionally, the metal is widely used as an adjuvant in vaccine preparations (5).

The irritant effects of Al salts to the skin vary considerably. Sensitivity reactions to Al are very rare. Recently, however, desensitization of hay fever patients with Al-precipitated allergens has been found to cause contact sensitivity to Al. Sensitization occurs during continuous application of Al adjuvants in vaccines and pollen extracts (8).

Therefore, in the present study, the Al contents of 18 patch test allergens were measured by atomic absorption spectrophotometry.

METHODS

Reagents and Solutions

Throughout the study deionized and distilled water was used for washing and standard preparations. Supra pure grade nitric acid (Merck) was used for the pre-treatment procedure of the Al sample. A 1,000 ppm certified atomic absorption Al standard solution (Sigma) was used to prepare working standards.

The standard solutions of Al were prepared with 1% nitric acid at concentrations such as 15.0, 30.0, 45.0, and 60.0 ng/mL. All standard solutions were prepared daily.

Sample Collections and Preparation

The several patch test allergens were obtained from the Dermatology Clinic at Hacettepe University Hospital. They are all manufactured by the same medical supply company and commonly used in Turkey.

The samples from the patch test allergens were weighed by a balance (Mettler AT-201), then 2.0 mL nitric acid (Merck) and 0.5 mL hydrogen peroxide (Merck) were added to each sample. Following this, the samples were placed on Milestone Microwave Digestion Unit (MLS-1200 MEGA) for acid digestion.

Aluminum Measurements

Each digested sample was used for Al measurements. Determinations of Al were performed on a Varian 30/40 atomic absorption spec-

Table 1
Microwave Program for Digestion of Samples to Al

Step No	Time	Power
1	00:01:00	250
2	00:01:00	0
3	00:05:00	250
4	00:05:00	400
5	00:05:00	650
Vent: 00:05:00	Rotorcil on	Twist on
Rotortype: HDR-1000/6		
Vesseltype: TFM		

trophotometer, a Varian GTA96 graphite tube atomizer, and a Varian DS-15 data station. The graphite furnace was purged with prepurified argon gas, during the furnace's operation, the gas "stop condition" was used only during the atomization step. A Varian auto sampler was used to inject 10 μ L aliquots of sample solution. Pyrolytically coated graphite tubes (i.d. 5.8 mm; o.d. 80 and 28.0 mm) were used. The mixtures were transferred to the sampler of the graphite furnace, and the results were taken from the printer after starting the furnace program. Results were given as micrograms of Al per gram of dry allergen (μ g/g).

RESULTS

Table 1 shows the microwave program, and Table 2 shows the instrument parameters and furnace program for Al measurement. In the present study Al content in 18 patch test allergens were determined by atomic absorption spectrophotometer. It was found that Al levels in the preparations tested in this study ranged from 7.13 to 57.19 μ g/g. The results are shown in Table 3.

DISCUSSION

Al salts are used in the preparation of a number of vaccines, toxoids, and allergen injectants as a common adjuvant. These Al salts are used during the preparation of biological compounds to absorb the antigenic components of the injectants and also to serve as adjuvants, which enhance the antigenicity of the materials after administration. Federal regulations in the United States (US Code of Federal Regulations, 1982) limit the individual dose of Al in biological injectants to a maximum of

Table 2
Instrument Parameters and Furnace Programs
for Al Determination

Instrument Parameters			
Lamp current (mA)		10	
Slit width (nm)		0.5	
Slit height		Normal	
Wavelength (nm)		309.3	
Measurement time (sec)		3.2	
Replicates		2	
Background correction		off	
Furnace Parameters			
Step No	Temperature (°C)	Time (sec)	Gas flow (l/min)
1	75	5.0	3.0
2	90	20.0	3.0
3	250	10.0	3.0
4	250	10.0	3.0
5	1400	10.0	3.0
6	1400	20.0	3.0
7	1400	3.0	0.0
8	2450	1.2	0.0
9	2450	2.0	0.0
10	2700	2.0	3.0

0.85 mg Al, or 1.14 mg Al, if the Al content is calculated on the basis of the amount of Al added during the preparation of the injectant (5). Al-precipitated allergenic extracts are made by complexing conventional allergenic materials with the metal. The resulting products afford more gradual absorption of the allergen, thereby reducing the risk of immediate adverse reactions. Reactions to Al vary from extremely rare allergic contact dermatitis and granulomas, to rather frequent irritant dermatitis, to exotic porphyries in patients with renal failure (9).

Subcutaneous nodules have been reported in patients receiving Al-containing extracts. Al allergy should always be suspected when red infiltrated annular rings are seen after patch testing with Al Finn chambers (10–12). However, irritant reactions can also occur, so sensitization should be confirmed by patch testing with a series of Al allergens,

Table 3
The Al Content of Allergens Used in Patch Tests

Number of Sample	Type of Sample	Al Content (Mean value, as $\mu\text{g/g}$)
1	Balsam of Peru (25 %)	26.38
2	Benzocaine (5 %)	31.14
3	Black Rubber mix (previous PPD mix, 0.6 %)	20.82
4	Cobalt chloride (1 %)	37.68
5	Colophony (20 %)	21.36
6	Epoxy resin (1 %)	18.69
7	Ethylendiamine dihydrochloride (1 %)	57.19
8	Fragrance mix (8 %)	14.46
9	Mercapto mix (2 %)	16.96
10	Neomycin sulphate (20 %)	7.13
11	Nickel sulphate (5 %)	18.31
12	Paraphenyldiamine free base (1 %)	55.14
13	Paratertiary Butylphenol Formaldehyde Resin (1 %)	23.09
14	Potassium dichromate (0.5 %)	15.72
15	Quaternium (1 %)	27.56
16	Quinoline mix (6 %)	25.32
17	Thiuram mix (1 %)	8.67
18	Wool alcohol (30 %)	39.99

using plastic chambers. Serial patch testing with Al allergens should be performed in patients developing eczematous or strong local reactions during hyposensitization with Al-precipitated allergens or vaccines containing Al adjuvants. Furthermore, Al sensitivity should be suspected in patch test using Finn chambers if contact sites show red infiltrated papular rings (8). Al Finn chambers do not themselves seem to sensitize, but this could be due to their brief application period (11).

The typical time course for subcutaneous Al absorption has not been characterized. If some Al can be rapidly absorbed from the site of vaccine administration, the neurotoxic properties of Al could contribute to the onset of a postvaccination encephalopathy. Some investigators have

suggested that abnormal accumulations of Al in the human brain may occur as a secondary consequence of other primary pathogenic events (5).

Reactions at the injection site are well known in children from the vaccines or at sites of hyposensitization therapy with Al-containing allergen extracts and may represent a potential risk for developing persistent Al-containing pruriginous nodules at the injection sites, and the appearance of such nodules may be associated with Al hypersensitivity. The dose of Al upload causing an Al-sensitivity reaction is not clear (12).

The presence of Al in patch test allergens may interfere with the diagnosis and evaluation of response of patients to allergens. Eighteen test allergens, whose prospectuses did not give any information about their Al contents, were assayed in the study. We found that the Al content in these allergens ranged from 7.13 to 57.19 µg/g. However, it is difficult to say that the Al content in individual dose of the patch test allergen tested in our study is high or low. Al-sensitivity risk should be considered while using the allergens that contain Al, no matter what the Al level is in the individual dose.

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