

Occupational contact urticaria caused by cyclic acid anhydrides

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Background: Cyclic acid anhydrides often cause allergic respiratory diseases, but contact urticaria because of these anhydrides has been considered rare.

Objective: We describe 21 patients diagnosed with occupational contact urticaria at the Finnish Institute of Occupational Health during the period 1990–2006.

Method: Prick test with human serum albumin (HSA)–acid anhydride conjugates, determination of specific immunoglobulin E (IgE), and open application were used in the diagnosis.

Results: The majority of the patients worked in the manufacture of electrical machines and were exposed to an epoxy hardener containing methyl hexahydrophthalic anhydride. The largest prick test reaction was often noted for the acid anhydride the patient had been exposed to. The specific IgE results were mostly in line with the prick test reactions. Phthalic anhydride IgE was determined in 20 patients and was found positive in 19 patients. In open application, a positive test result often required the use of the undiluted hardener.

Conclusions: Contact urticaria may be more common than previously believed. Prick tests with HSA–acid anhydride conjugates were a useful test method for detecting immediate sensitization to acid anhydrides. The determination of the specific IgE gave almost equal results. The open application test often had to be performed with the undiluted anhydride product to obtain a positive test result.

Key words: chlorendic anhydride; immediate allergy; maleic anhydride; methyl hexahydrophthalic anhydride; methyl tetrahydrophthalic anhydride; open application test; phthalic anhydride; prick test; specific IgE. © Blackwell Munksgaard, 2009.

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Cyclic (organic, dicarboxylic) acid anhydrides are synthetic, highly reactive low-molecular chemical compounds that are widely used as curing agents for epoxy resins and in the production of polyester and alkyd resins (1). The acid anhydrides appear as liquids or in crystal form depending on the type of the anhydride. Commonly used acid anhydrides (Fig. 1) are phthalic anhydride (PA; CAS 85-44-9), maleic anhydride (MA; CAS 108-31-6), trimellitic anhydride (TMA; CAS 552-30-7), tetrahydrophthalic anhydride (THPA; CAS 85-43-8), hexahydrophthalic anhydride (HHPA; CAS 85-42-7), methyl hexahydrophthalic anhydride (MHHPA; CAS 25550-51-0), and methyl tetrahydrophthalic

anhydride (MTHPA; CAS 26590-20-5). Workers may be exposed to acid anhydrides in powder or liquid form during various manufacturing processes. Exposure to acid anhydride fumes may also occur in hot processes, such as the heat hardening of epoxy resins (2). Cyclic acid anhydrides react easily with water forming the corresponding acids, which irritate skin and respiratory membranes. In addition to their irritating effects, acid anhydrides are well known for their ability to cause respiratory immunoglobulin E (IgE)-mediated sensitization and occupational allergic diseases such as rhinoconjunctivitis and asthma (3–8).

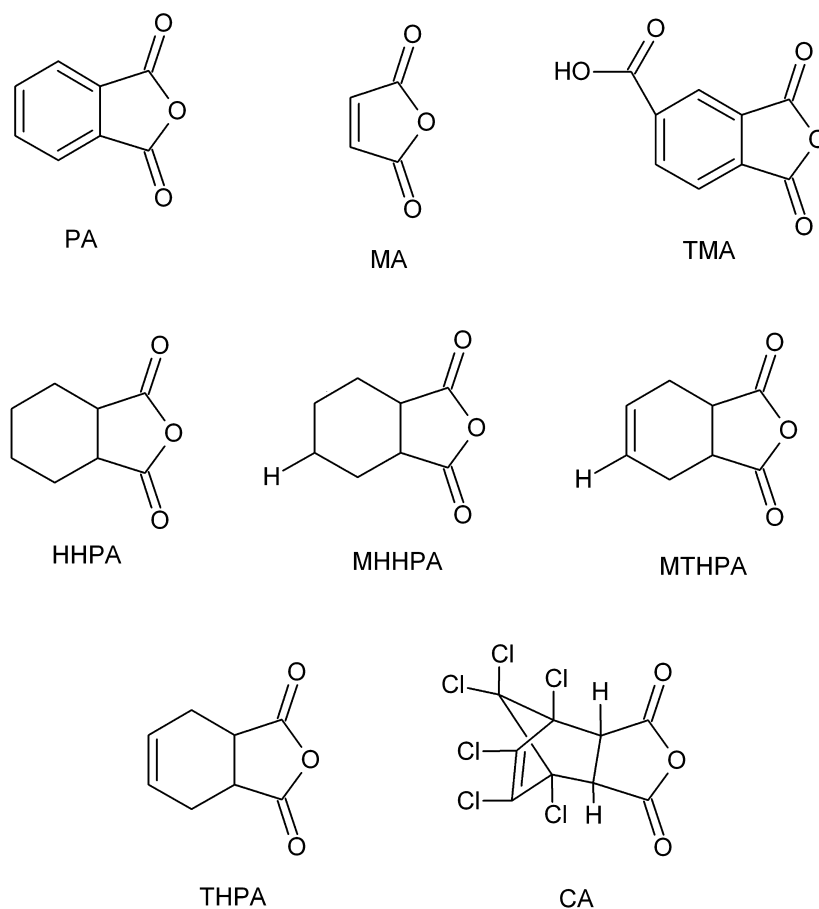


Fig. 1. Structural formulas of cyclic acid anhydrides. CA, chlorendic anhydride; HHPA, hexahydrophthalic anhydride; MA, maleic anhydride; MHHPA, methyl hexahydrophthalic anhydride; MTHPA, methyl tetrahydrophthalic anhydride; PA, phthalic anhydride; THPA, tetrahydrophthalic anhydride; TMA, trimellitic anhydride.

In the literature, acid anhydride contact urticaria has been described in case reports of single or few patients. Baader and Menschick gave the first reports on urticarial reactions among workers in the production of PA (9, 10). A case of contact urticaria caused by PA was recently described in a refinery worker in Spain (11). A case of contact urticaria because of exposure to an epoxy resin hardener containing MHHPA in an electrical factory worker was described by Jolanki et al. (12). Subsequently, contact urticaria caused by occupational exposure to epoxy resin hardeners containing MHHPA, HHPA, and MTHPA has been described in four cases at the Finnish Institute of Occupational Health (FIOH) (13–15). In Japan, one worker with occupational exposure to MHHPA and HHPA had widespread urticaria and showed specific IgE antibodies to PA and HHPA (16). In Finland, exposure to MA caused contact urticaria in a process operator in the production of polyester resin (17), and chlorendic anhydride (CA) in welding fumes of polyester paint was the reason for contact urticaria in an assembler (18).

Delayed contact allergy to acid anhydrides is even rarer. A case of allergic contact dermatitis from dodecenyl succinic anhydride in a laboratory

technician was reported by Goransson (19). A horizontal boring-machine worker developed both allergic contact dermatitis and allergic rhinitis by exposure to MHHPA (20). In addition, two ceramic workers in Italy had contact allergic reactions to MA (21).

In this report, we present the data of 21 patients diagnosed with occupational acid anhydride contact urticaria who were examined at the FIOH during the period 1990–2006. Five of the patients have been described in previous reports (14, 15, 17, 18).

Material and Methods

We retrospectively reviewed the patient and test files of FIOH for the period 1990–2006 to find patients who had been diagnosed with occupational contact urticaria because of exposure to organic acid anhydrides. We found 21 such patients. The majority of the patients were male (16; 76%), and the mean age of the patients at the time of the diagnosis was 37 years. Seven patients had a history of atopic symptoms (asthma, hay fever, and childhood eczema).

From their medical records, we collected data on occupation and work tasks, occupational

exposure to acid anhydrides, work-related symptoms, results of the clinical examinations and immunological tests performed at FIOH, and diagnoses of occupational diseases.

At FIOH, the examination of a patient with a suspected occupational IgE-mediated allergic disease from acid anhydrides consists of prick testing with a series of different acid anhydrides. We use hapten conjugates of acid anhydrides and human serum albumin (HSA), which have been prepared according to the method of Howe et al. (22). Prick test reactions of a minimum diameter of 3 mm and at least half the size of the histamine-positive control reaction are regarded positive. A prick test series of acid anhydrides has been used at FIOH since 1990. Initially, the series contained the acid anhydrides PA, MA, TMA, MHHPA, and MTHPA. HHPA was included in 1994 and CA in 1999. MTHPA has not been used in the series since 2004 because of its constant cross-reactivity with other acid anhydrides and cost. During the period 1990–2006, prick tests with the series of acid anhydrides were performed at FIOH on 602 patients and positive test reactions to one or several acid anhydrides were noted in 87 patients.

In addition to prick testing, determination of specific IgE is frequently used at FIOH to confirm sensitization. During the study period, several different commercial methods as well as in-house radioallergosorbent test methods for the determination of IgE to acid anhydrides were used. We currently use ImmunoCAP 100 (Phadia AB, Uppsala, Sweden).

At FIOH, the diagnosis of occupational contact urticaria caused by acid anhydrides is often confirmed by an open application test with the substance suspected of causing the reaction of contact urticaria. Open application with an anhydride product is performed only in prick-positive patients. We used either the same acid anhydride–HSA conjugate as in the prick test or the acid anhydride-containing product from the workplace. The product, usually a hardener, is either used 'as is' or diluted to the desired concentration, and the vehicle, water, petrolatum (pet.), or ethanol is used as control. When the acid anhydride–HSA conjugate is used in the open test, HSA is used as control. The dilutions in water, ethanol, or pet. are prepared on the same day before the test in small plastic containers by mixing with a wooden stick, and the lids of the containers are shut and the test substances are left to wait for the test. In the open application, the test substance is applied thinly with a cotton bud to a 5 × 5 cm area on the healthy skin of the forearm and left uncovered. After 20 min, the skin surface is inspected by a dermatologist and the applica-

tion is repeated to the same area. After 40 min, the test is read again, and then, the test material is removed and the skin is washed. The use of two applications at a 20-min interval and reading at 20 min after each application is a routine for all open applications at FIOH. A reaction with one or several urticarial wheals in the application area without a simultaneous reaction in the control area is considered positive.

Patch tests are used to detect possible concomitant delayed sensitization to epoxy compounds or other allergens. When a patient has had only immediate skin symptoms during the workday that disappear within a few hours, patch tests are usually not performed.

Results

Of the 21 patients, 9 had one or several positive reactions in the standard prick test series of common environmental allergens. Total IgE (ImmunoCAP 100 Total IgE; Phadia AB) was measured in 19 of the patients. The range of total IgE was 8–967 kU/l and median was 83 kU/l as only seven in the group had a total IgE over the reference value of 110 kU/l.

The patients' occupational exposure to acid anhydrides and the diagnosed occupational diseases are described in Table 1. In 19 patients, the exposure was determined according to the safety data sheet of the product used at the workplace. Two of the patients were welders who had been exposed to welding fumes of paint containing acid anhydrides. In the previously reported case of immediate allergy to CA, chemical analysis identified CA and PA in the welding fumes of the heated paint (18). In the other case, the patient had been exposed while welding pipes coated with an anti-rust paint that probably releases PA when heated. The mean exposure time before symptoms was 5 years.

Sixteen of the patients also had allergic rhinitis caused by an acid anhydride and 5 patients had occupational asthma because of an acid anhydride. Three patients reported that the symptoms of contact urticaria had been the first symptoms, and in five cases, rhinitis was reported as the first symptom. In the rest of the cases, the skin and respiratory symptoms were reported to have arisen simultaneously.

Table 2 presents the results of the prick tests with different acid anhydrides compared with the respective specific IgE.

In 11 of the cases, open application tests were performed after prick testing, and the results are presented in Table 3.

Seven of the patients had contact urticaria exclusively on the hands and forearms from

Table 1. Occupation, business area, anhydride causing contact urticaria, and diagnosed occupational respiratory diseases (caused by acid anhydrides) of the 21 patients with occupational anhydride contact urticaria

Patient number	Occupation	Business area	Anhydride causing contact urticaria	Anhydride rhinitis	Anhydride asthma	Reference
1	Winder	Manufacture of electrical machines	MHHPA	+	—	(15)
2	Installation worker	Manufacture of electrical machines	MHHPA	—	+	
3	Production line worker	Capacitor production	MHHPA	+	—	
4	Production line worker	Microelectronics	MHHPA	—	—	
5	Winder	Manufacture of electrical machines	MHHPA, HHPA	+	—	
6	Chimney sweeper	Manufacture of electrical machines	MHHPA	—	—	
7	Installation worker	Manufacture of electrical machines	MHHPA	+	—	
8	Electrician	Manufacture of electrical machines	MHHPA	+	—	
9	Winder	Manufacture of electrical machines	MHHPA	+	—	
10	Installation worker	Manufacture of electrical machines	MHHPA	+	—	
11	Winder	Manufacture of electrical machines	MHHPA	+	—	(14)
12	Installation worker	Manufacture of electrical machines	MHHPA	+	—	
13	Electrician	Manufacture of electrical machines	MHHPA	+	+	
14	Impregnator	Manufacture of electrical machines	MHHPA	+	—	
15	Packer	Production of sports equipment	MHHPA, MTHPA	+	+	(14)
16	Production line worker	Production of sports equipment	MTHPA	—	—	
17	Production line worker	Electronics	MTHPA	+	—	
18	Packer/storage worker	Warehouse	PA	+	+	
19	Plumber/welder	Plumbing	PA	+	—	
20	Process operator	Polyester production	MA	+	—	(17)
21	Assembler/welder	Manufacture of forestry machines	CA	—	+	(18)

CA, chlorendic anhydride; HHPA, hexahydrophthalic anhydride; MA, maleic anhydride; MHHPA, methyl hexahydrophthalic anhydride; MTHPA, methyl tetrahydrophthalic anhydride; PA, phthalic anhydride.

handling products containing acid anhydrides. Five patients experienced urticaria symptoms only in the face and neck. Six patients had more widespread symptoms on the bare areas of the skin on the face and upper limbs. In two patients, their urticaria had also spread to covered skin areas.

We noted no cases of severe generalized urticaria with systemic symptoms (Table 4).

Patch tests had been performed on 11 patients. Seven patients were patch tested with the acid anhydride-containing product diluted to a concentration of 0.125–2% from the workplace. No

Table 2. Results of prick tests and determination of specific IgE^a

Patient number	Anhydride used at the workplace	PA		MA		TMA		MHHPA		MTHPA		HHPA		CA	
		Prick (mm)	IgE (kU/l)	Prick (mm)	IgE (kU/l)	Prick (mm)	IgE (kU/l)	Prick (mm)	IgE (kU/l)	Prick (mm)	IgE (kU/l)	Prick (mm)	IgE (kU/l)	Prick (mm)	IgE (kU/l)
1	MHHPA	9	4.6	8	—	0	—	28	4.5	9	12.2	33	—	—	—
2	MHHPA	5	8.0	5	1.9	0	<0.3	11	—	7	15.1	9	15.5	3	—
3	MHHPA	0	2.3	3	1.2	0	<0.3	20	1.3	7	5.1	8	5.5	—	—
4	MHHPA	0	—	0	—	0	—	8	—	—	—	9	3.15	0	—
5	HHPA, MHHPA	7	14.9	9	—	4	—	10	—	10	—	10	—	—	—
6	MHHPA	5	0.46	0	—	0	—	9	—	7	2.53	6	2.0	0	—
7	MHHPA	0	3.9	0	—	0	—	10	1.7	6	—	6	4.0	0	—
8	MHHPA	0	0.5	0	—	0	—	14	—	—	2.44	18	1.67	0	—
9	MHHPA	0	1.7	3	0.4	0	<0.3	7	2.7	7	4.4	7	4.1	—	—
10	MHHPA	7	7.2	4	1.0	0	0.5	20	3.3	25	9.1	40	10.2	—	—
11	MHHPA	9	7.4	8	1.9	4	1.2	13	20.1	13	14.8	—	—	—	—
12	MHHPA	15	4.0	0	<0.3	4	—	21	3.1	6	6.3	7	—	—	—
13	MHHPA	11	8.3	6	2.3	6	1.0	13	9.4	12	18.8	13	14.9	6	—
14	MHHPA	0	1.3	0	<0.3	0	<0.3	5	0.6	4	2.0	6	—	—	—
15	MHHPA, MTHPA	10	>52.5	9	8.7	7	6.2	10	>52.5	9	>52.5	—	—	—	—
16	MTHPA	5	5.1	7	—	5	—	8	—	10	10.2	10	—	0	—
17	MTHPA	0	<0.3	0	<0.3	0	<0.3	5	<0.3	8	<0.3	8	—	—	—
18	PA	6	1.4	0	<0.3	0	<0.3	0	<0.3	0	<0.3	0	—	—	—
19	PA	4	0.7	0	<0.3	0	<0.3	0	<0.3	0	<0.3	0	<0.3	—	0
20	MA	0	2.4	14	9.4	0	—	0	—	0	—	0	—	—	—
21	CA	3	1.2	5	1.7	4	<0.3	6	1.1	6	2.9	6	2.4	10	120

—, not tested; CA, chlorendic anhydride; HHPA, hexahydrophthalic anhydride; IgE, immunoglobulin E; MA, maleic anhydride; MHHPA, methyl hexahydrophthalic anhydride; MTHPA, methyl tetrahydrophthalic anhydride; PA, phthalic anhydride; TMA, trimellitic anhydride.

^aThe anhydride causing the contact urticaria are indicated in bold.

Table 3. Results of open application tests^a

Patient number	Anhydrides used at work	Product used at work (%)					Acid anhydride–HSA conjugate (prick test substance)
		100	20	10	5	1	
1	MHHPA	+				+aq.	+
2	MHHPA						+
3	MHHPA			+aq.			
4	MHHPA	+		–eth.		–pet., eth.	
5	HHPA, MHHPA	+		–aq.		–aq.	
6	MHHPA		+pet.		–pet.		
7	MHHPA	+		?+aq.			–
8	MHHPA	+		–		–pet., eth.	–
9	MHHPA	+				–aq.	
20	MA	+				–aq.	+
21	CA						+

+, a positive reaction; ?+, a doubtful reaction; –, a negative reaction; aq., water as a vehicle; CA, chlorendic anhydride; empty box, not tested; eth., ethanol as a vehicle; HHPA, hexahydrophthalic anhydride; HSA, human serum albumin; MA, maleic anhydride; MHHPA, methyl hexahydrophthalic anhydride; MTHPA, methyl tetrahydrophthalic anhydride; PA, phthalic anhydride; pet., petrolatum as a vehicle.

^aThe test substance was either the actual product from the workplace (containing anhydrides) or the corresponding anhydride–HSA conjugate used in the prick tests.

contact allergic reaction to the products was noted. In addition, three patients were tested with a 1% dilution (in pet.) of MHHPA as a part of the epoxy resin patch test series, and they all showed a negative test result. One patient had a positive patch test to epoxy resin. One patient had been diagnosed with occupational epoxy resin contact allergy in earlier examinations but was not tested again at our institute. Three patients had contact allergic reactions that were considered non-occupational (nickel, cobalt, gold, benzyl salicylate, and fragrance mix).

Twenty of the 21 patients had attended a follow-up examination at our institute. All the patients

had changed work tasks after the diagnosis of allergy to acid anhydrides or even earlier; so they were no longer exposed, and their symptoms of contact urticaria had ceased by the time of the follow-up visit.

Discussion

Occupational contact urticaria caused by acid anhydrides has been considered relatively rare (4), and there have only been a few prior reports in the literature (11–18). Respiratory allergic symptoms because of acid anhydrides are, on the

Table 4. Location of urticaria in relation to exposure route

Patient number	Location of urticaria	Work task or the way of exposure	Principal route of exposure
1	Forearms, neck, face	Working near curing area (winder)	Airborne
2	Forearms	Mixing resin and hardener	Skin contact
3	Left hand	Handling recently cured capacitor parts	Skin contact
4	Face, left hand	Insulating components with epoxy resin	Skin contact
5	Chest, arms	Working near curing area (winder)	Airborne
6	Forearms	Cleaning curing ovens	Skin contact
7	Hands, forearms	Visits to curing area (winder), occasional skin contact	Skin contact
8	'Area of skin contact', location not described	Testing recently cured motors	Skin contact
9	Arms, body, legs	Working near curing area (winder)	Airborne
10	Hands	Handling recently cured capacitor parts	Skin contact
11	Face, neck, hands	Visits to curing area (winder)	Airborne
12	Face, neck, hands	Repairing equipment in curing area	Skin contact
13	Forearms	Handling recently cured motor parts	Skin contact
14	Hands, forearms	Insulating components with epoxy resin	Skin contact
15	Forearms, face	Packing, working near curing area	Airborne
16	Face	Manufacturing sports equipment	Skin contact
17	Face	Working near curing area (winder, production line worker)	Airborne
18	Face, neck	Packing PA in powder form	Skin contact
19	Face, neck	Welding painted pipes releasing PA	Welding fumes
20	Widespread urticaria, also covered skin area	Mixing MA and PA in polyester production	Skin contact
21	Face	Welding items painted with a polyester paint releasing CA	Welding fumes

CA, chlorendic anhydride; MA, maleic anhydride; PA, phthalic anhydride.

other hand, a well-known entity (3–8). In previous reports on respiratory allergy connected with acid anhydrides, patients' possible skin symptoms have not usually been mentioned. In our material, 24% or 21 patients of a of 87 prick test-positive individuals had symptoms and clinical findings diagnostic of contact urticaria because of acid anhydrides. This could point to the fact that contact urticaria is an under-diagnosed symptom in individuals exposed to acid anhydrides. The symptoms are usually mild and of short duration, and the patients do not necessarily bring them to their physician's attention. The urticaria is usually combined with allergic respiratory symptoms that are more frequently noticed. In our material, only three persons had contact urticaria without a simultaneous diagnosis of an allergic respiratory disease.

In our study, MHHPA was the most common acid anhydride responsible for the occupational exposure of the patients. A total of 15 of the 21 patients in our study had contact urticaria from MHHPA-containing curing agents for epoxy resin systems. Twelve of the patients had worked at a large Finnish company producing electrical machines for industrial use. The plant uses epoxy resins in the production process that demand a curing agent containing MHHPA, which was the agent causing the contact urticaria in all these 12 patients.

In the present series, there were seven patients whose contact urticaria symptoms were limited to hands and/or forearms, and these were all clearly connected to direct skin contact with anhydride products.

Six of the patients had not handled the product containing acid anhydrides themselves but had been exposed airborne from processes in the adjacent working environment. Airborne exposure usually resulted in more widespread urticaria than direct skin contact. Welding fumes represent a specific form of airborne exposure. Two of the patients developed contact urticaria affecting the face because of exposure to the welding fumes from painted items containing acid anhydrides. One of the patients (number 19) was a plumber who was exposed while welding pipes coated with an anti-rust paint that releases PA when heated. The other case, a welder who developed contact urticaria from exposure to CA in welding fumes (number 21), was described in an earlier FIOH report (18).

In our material, a total of eight (38%) patients had airborne contact urticaria from anhydrides. Our result does not contradict the assessment that airborne exposure, in general, is underestimated as a skin exposure route (23).

Prick tests

The prick test results show a good correlation with occupational exposure: all patients had a positive prick test reaction against the acid anhydride they were exposed to.

All the 15 patients diagnosed with contact urticaria because of exposure to MHHPA had positive prick reactions against MHHPA. The curing agents used in epoxy resin systems usually also contain traces of HHPA, which could explain the positive prick reactions against HHPA in all the 13 MHHPA-exposed patients who were tested with HHPA. Thirteen of these patients also had a positive reaction against MTHPA in the prick tests. MHHPA is also known to contain traces of MTHPA, which can explain these findings (1). Another explanation for the simultaneous positive prick test reactions could be cross-reactivity because of the similar chemical structure of the substances. The results in previous studies on respiratory sensitization have been in line with these findings, and cross-reaction has usually been considered the most likely explanation (24, 25).

The two patients exposed to PA did not show any positive prick test reactions to the other tested acid anhydrides in the series, and the patient exposed to MA only had positive prick test reactions to PA and MA. Also, in other studies, PA has shown less cross-reactivity than the other acid anhydrides (25).

Specific IgE

Determination of specific IgE to some acid anhydride was performed on all the patients, but five patients exposed to MHHPA had not been tested for specific IgE to MHHPA. Specific IgE antibodies to the acid anhydride at the workplace were determined in 16 of the patients; only 1 of the tested patients did not show specific IgE antibodies to the anhydride used at work. The results of the specific IgE correlated well with the exposure and prick test results. Similar findings have been reported in earlier studies (24–28). Specific IgE antibodies for PA were determined in 20 patients and were positive in 19, regardless of which acid anhydride the patient had been exposed to, and thus serve as a useful screening method for sensitization to acid anhydrides.

Open application test

Open application was performed on 11 of the 21 patients. All the patients who underwent open application showed a positive test result. It is noteworthy that a clear positive urticaria reaction required the use of the undiluted curing agent in

seven of the nine patients who were tested with their own product. One patient reacted to the 1% dilution and another to the 10% dilution of the product. Two of the patients were tested with only the acid anhydride–HSA conjugate, which gave positive test results.

Of the previously reported FIOH cases not included in this report, the first patient was only tested with the undiluted MHHPA hardener, which gave a positive result in the open application (12). The other patient was tested with both 100% and 1% MHHPA, and both open application tests were positive (13). In their study, in addition to specific IgE determination, Yokota et al. used a 20-min closed patch test with the undiluted acid anhydride, which gave a positive test result for MHHPA (16).

With the open application, we try to show the clinical relevance of a positive prick test. It is meant to be a skin provocation and an organ-specific provocation similar to nasal and bronchial provocations. A positive skin provocation (open application test) is not, however, a requisite for a diagnosis of occupational contact urticaria at FIOH. Skin permeability may be increased because of irritant factors or, for example, atopic dermatitis, and these factors may vary a lot. The test can be negative when the skin has healed.

This is a retrospective material, and we describe what has been carried out with the patients. In our current opinion, the use of water as a vehicle of anhydrides is not rational; the anhydrides probably react with water immediately. Ethanol also contains some water, so its use is not a better alternative. The use of water-containing vehicles would have explained the negative results to the dilutions, but all the water dilutions were not negative. This might point to the possibility that at least in such cases, the hapten is not the anhydride but some other structure. We have not checked the anhydride content of the water, ethanol, or pet. dilutions. The anhydride–HSA conjugates, in turn, are quite well characterized: each HSA molecule contains about 30 anhydride molecules (the solution is 1% for HSA). On the other hand, the use of anhydride–HSA conjugate in the open application test does not add much to the prick test; it is simply a skin permeability test to the protein conjugate. At work, the patient does not have skin contact with the conjugate but with a product that contains the anhydride itself. The negative open application tests with anhydride–HSA conjugates were probably because of the large size of the conjugate resulting to poor penetration into the skin.

On the basis of the present retrospective material, it is difficult to give definite recommendations on how the open application should be performed.

Although the positive reaction often required the use of undiluted product, we do not recommend starting the test with the product itself. We ourselves continue diluting an anhydride product in pet. (1% and 10%) before applying the undiluted product. The application of the product resembles the situation in the workplace where the workers every now and then have direct skin contact with the product. With the gradual approach, we want to avoid any strong reactions that might appear, for example respiratory symptoms.

In Finland, the insurance companies favour provocation tests, and with a positive skin provocation (open application test), it is easier to have the disease recognized and for the patient to receive compensation. For centres unfamiliar with the open application test, determination of specific IgE serves as a useful tool to diagnose the contact urticarias. The HSA conjugates, if available, are also useful. Anhydride contact urticaria itself is often of minor clinical importance (symptoms are mild, transient, and often easily avoided with proper gloves and long sleeves), but it is important to diagnose the immediate sensitization and investigate possible respiratory symptoms.

Recommendations for the workplace

If a worker has been occupationally sensitized to acid anhydrides and has contact urticaria symptoms, it is advisable to transfer him/her to a task where he/she is no longer exposed to anhydrides because of the risk of developing asthma – in the worst case a chronic disease. The large electric company responsible for the majority of the Finnish patients had usually already transferred the sensitized workers to another department before investigations at FIOH.

In conclusion, we believe that contact urticaria is more common in those individuals exposed to acid anhydrides than previously noted, and contact urticaria can be the first clinical symptom of sensitization. More attention should be given to skin symptoms in the examination of exposed persons. Prick testing and specific IgE can be used to identify sensitized persons, and the diagnosis of contact urticaria can be confirmed by an open test. The open application often has to be performed with the undiluted anhydride product to achieve a positive test result.

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