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Hideo Nakayama M.D.^α, Akiko Kumei M.D.^σ, Ko Ron Chen M.D. & Masatoshi Takaoka, PhD.^ω

Abstract- There is enough accumulated evidence to conclude that house dust mites (HDM) are the most significant causes of atopic dermatitis (AD). HDMs are known to increase serum IgE and RAST scores for Dps and Dfs, and will often show positive results among AD patients when a patch test using three crushed HDMs or a petrolatum-base test using many HDMs is performed.

However, HDMs are invisible to the naked eye as they measure less than 0.3 mm, and therefore even when thousands of HDMs are present in the interior of the patients' homes, they live quietly without causing any noise, and therefore their presence cannot be detected by the patients.

The newly developed Methylene Blue Agar method (MBA) can reveal how many HDMs are present in each household furniture, and through this method, they can be reduced to less than 50/m² per 20seconds aspiration for all furniture and mattresses, dramatically improving severe symptoms of AD for patients who have even suffered for more than ten years.

Therefore, it is critical that the mite fauna of the patients' home is examined so that effective measures can be taken to cure the patient. Furthermore, AD is considered as a unique form of allergic contact dermatitis due to the fact that HDMs involve both type I and type IV allergies. Please note that there are also rare cases of AD which are caused by reactions towards metals and the malassezia group fungi.

Keywords: atopic dermatitis, house dust mite (HDM), mite allergy, mite fauna, α-acaridial.

I. INTRODUCTION

Atopic dermatitis (AD) is a commonly seen itchy recurrent dermatitis, present in many countries throughout the world. When the symptoms of an AD patient are so severe and generalized, in many cases it is intractable due to the fact that the true causations have been unknown to the patient. What is the best method of treatments for such severe cases? Is it the temporal improvement often provided by hospitals and clinics that consist of topical or systemic

usage of corticosteroid hormones and perorally administered antihistamines that quickly lose effect once the treatment is stopped? The answer is NO.

What patients with intractable severe AD want are skin conditions without erythema, papules, prurigoes, xerosis and itching, so that they no longer need to keep scratching themselves. Is it possible to provide such an ideal effective treatment? The answer is YES. This article will show you just how such a treatment is possible. Even though this fact has been known for more than 20 years [1,2,3], this information has not been spread widely enough partly due to the fact that institutes have only investigated the mite fauna among AD patients' houses in Tokyo and Chiba prefecture, and also the fact that the mite-free mattresses that the patients sleep in to effectively avoid contact of house dust mites (HDM) have only been sold in Japan.

Therefore, the authors wish to enlighten dermatologists who have had failed attempts at treating severe intractable cases of generalized AD through this article. We will show you 8 typical cases of AD patients who were all hypersensitive to HDM and had high values of serum IgE and RAST, and just how they were able to successfully be cured of severe eczema and prurigo on the skin (Fig. 1-8) through the remarkable effects of eliminating HDM to less than 50/m² per 20 seconds aspiration by a 320W vacuum cleaner and maintaining a clean environment.

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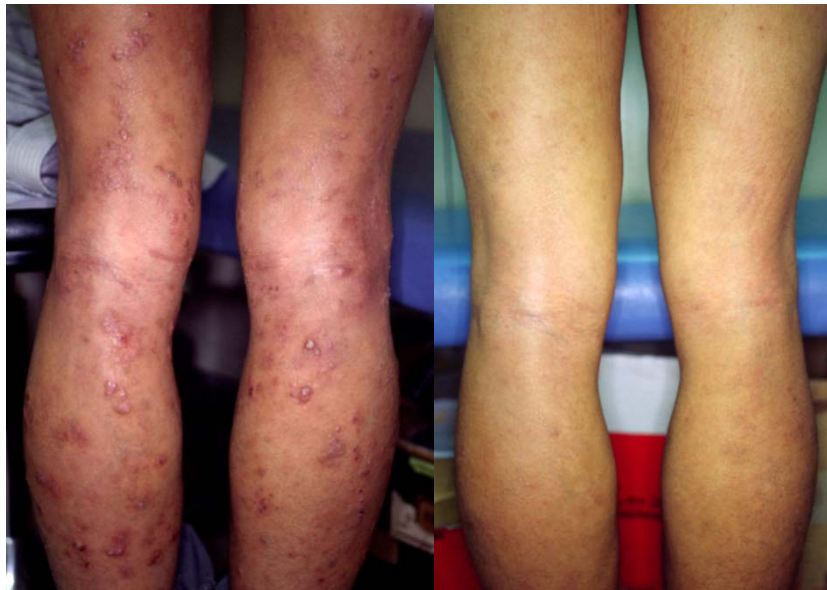


1a

1b

Fig. 1: (Color)

1a: 22-year-old man suffering from severe atopic dermatitis since childhood before receiving mite elimination.
1b: He was able to maintain a cured state for 4 months by reducing the number of mites in all household furniture to less than 50/m² per 20 seconds of aspiration.



2a

2b

Fig. 2: (Color)

2a: 29-year-old man suffering from severe atopic dermatitis since childhood before receiving mite elimination.
2b: He was able to maintain a cured state for 3 years by reducing the number of mites in all household furniture to less than 50/m² per 20 seconds of aspiration.



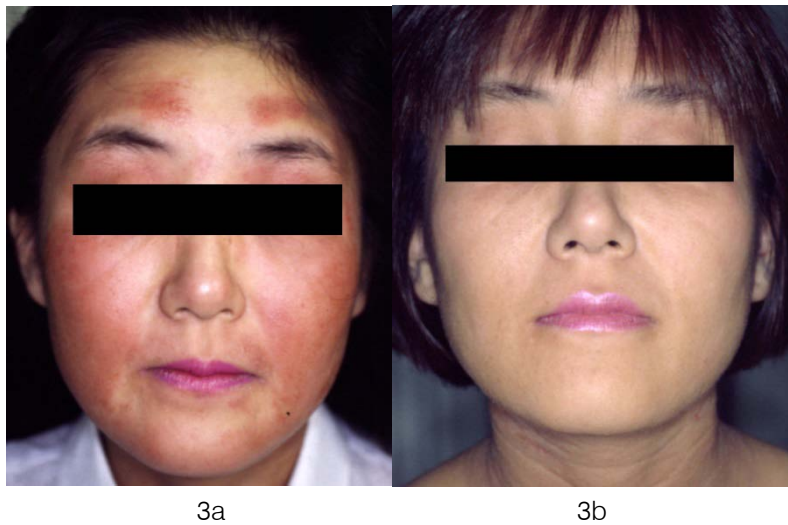


Fig. 3: (Color)

3a: Face of a 27-year-old woman suffering from severe atopic dermatitis before receiving mite elimination.

3b: She was able to maintain a cured state for 2 years and 11 months by reducing the number of mites in all household furniture to less than 50/m² per 20 seconds of aspiration.

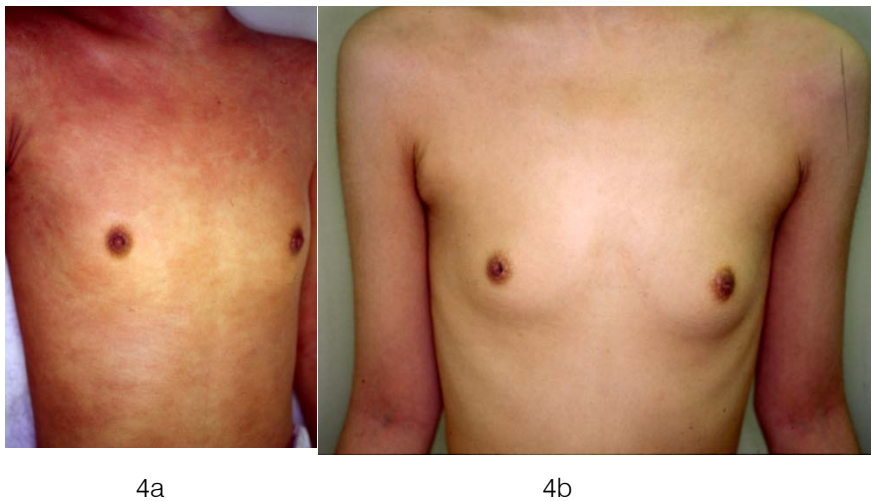


Fig.4: (Color)

4a: 23-year-old woman suffering from severe atopic dermatitis for more than 10 years before receiving mite elimination.

4b: She was able to maintain a cured state for 5 months by reducing the number of mites in all household furniture to less than 50/m² per 20 seconds of aspiration.



5a

5b

Fig. 5: (Color)

5a: 18-year-old man suffering from severe atopic dermatitis since 3 years before receiving mite elimination.

5b: He was able to maintain a cured state for a year and a half by reducing the number of mites in all household furniture to less than 50/m² per 20 seconds of aspiration.



Fig. 6: (Color)

6a: 19-year-old woman suffering from severe atopic dermatitis since 5 years before receiving mite elimination.

6b: She was able to maintain a cured state for a year and 4 months by reducing the number of mites in all household furniture to less than 50/m² per 20 seconds of aspiration.



7a

7b

Fig. 7: (Color)

7a: 28-year-old man suffering from severe atopic dermatitis for more than 10 years before receiving mite elimination. 7b: He was able to maintain a cured state for a year and 10 months by reducing the number of mites in all household furniture to less than 50/m² per 20 seconds of aspiration.



Fig. 8: (Color)

8a: 20-year-old woman suffering from severe atopic dermatitis for many years before receiving mite elimination. 8b: She was able to maintain a cured state for 3 months by reducing the number of mites in all household furniture to less than 50/m² per 20 seconds of aspiration.

These cured patients were delighted and thankful for having been able to eliminate the mites in their home environment through a scientific mite fauna investigation and being able to maintain their cured states. Allow us to introduce the remarkable effects and then explain to you the mechanism behind the treatment.

II. A BRIEF HISTORY OF ATOPIC DERMATITIS (AD) AND HOW HOUSE DUST MITE ALLERGY AMONG ATOPIC DISEASES WAS DISCOVERED

a) *The long history of AD*

The history of AD goes back as far as when human beings first set up countries all across the world. The first description of AD is said to have been the first

Roman Emperor Augustus (BC 63 - AD 14) who frequently scratched his skin due to eruptions which were accompanied by coughs and a runny nose [4]. Due to this unique trias, he is suspected as being the first AD patient in history. Augustus was an important successor of the famous Julius Caesar, but due to this disease, he was not as mighty as Caesar and ended up getting severely wounded after losing two battles. However, as Augustus excelled in politics, Caesar ordered him to concentrate in politics while military matters were succeeded to the young Agrippa. This division of work was successful in having established the new Roman Empire which would remain for almost 300 years (PaxRomana) [5]. The etymology of the term "eczema" comes from the Latin word "eczeo" which refers to something that is coming out from the skin.

In China, the same disease appeared in a medical textbook as the “wet eruption” in AD 610 [6]. Later it would be called “Nai-cheng” in 1617 by Chen Sa Kong who named it to mean “an eruption due to the mother’s milk” [7]. It was apparently differentiated from ordinary allergic contact dermatitis (“Pi-Fu-Yeng” in Chinese) because the swelling symptoms and the affected locations differed from “Nai-cheng”. As in the case of Fig. 9 when the same type of dermatitis was found on both the mother and baby’s cheeks, the causation was attributed to the mother’s milk or the disease was suspected as being hereditary.



Fig. 9 :(Color)

The presence of such cases, a 6 months old baby produced similar itchy eczema as her mother had on the face, suggested the causation was attributed to mother’s milk, or the disease was suspected as hereditary.

In 1923, Coca conceived the new medical term “Atopy” to imply human hereditary allergic diseases including eczema, bronchial asthma and hay fever. Dr. Marion Sulzberger once told the author in person that it was back in 1928 when he conceived to create the new term “atopic dermatitis” by introducing the adjective “atopic” for the first time. Prior to Sulzberger, AD had been referred to as “Asthma-eczema (Jadassohn)”, “Endogenes Ekzem (Korting)”, and “Constitutional prurigo-eczema (Bonnievie)” because the true mechanism had not yet been known. The term AD would only start to prevail after World War II in the 1950s. Dr. Marion Sulzberger also invented hydrocortisone ointment for the first time in the world. Many types of corticosteroid ointment followed and they were successful in temporarily improving severe eczema of AD but unable to prevent the relapse or generalization of these conditions.

b) *The gradual discovery of the mechanisms of AD*

In 1966, Ishizaka and his wife investigated atopic reagin among serum in Denver and discovered the new immunoglobulin “IgE” for the first time in the world [8]. As they knew that atopic reagin is abundantly contained in the serum of chronic flexor eczema patients, which in Japanese is “Kusa”, and that this disease was surely typical AD, the “E” in IgE might have from “eczema” but this was not ascertained by the authors when they met Dr. Ishizaka.

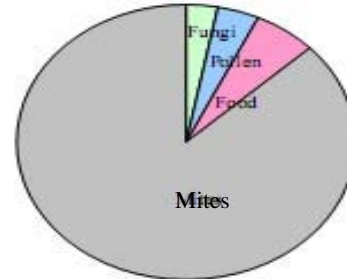
In 1970, Gunner et al reported that serum IgE specifically increased in the serum of AD patients [9]. The introduction of radio isotope soon clarified that the causative allergens raised serum IgE, but measuring specific IgE with more than 17.5 UA (Unit of allergy) of serum had been restricted for almost 20 years to avoid the excess exposure to isotopes for the employees in the laboratory. Therefore, patients with AD whose specific IgE by radio-allergo-sorbent-test (RAST) was as high as 500 UA to 2,000 UA to dermatophagoides were officially reported as being >17.5 UA. Later it was improved to >100 UA, but the true high values of UA had not been reported till 1989.

In 1989 a national project to find out the real causation and a truly effective treatment of AD began and it was executed by two medical schools and one educational hospital in Japan. To meet this specification, SRL the biggest medical laboratory in Tokyo was requested to dilute serum ten times when the RAST results were to be reported as >17.5 UA. When the results of 10 times dilution showed 14 UA, the real specific IgE was 140 UA, and when this dilution again showed >17.5 UA, dilution was performed 10 more times. If the result showed the value of 13 UA, the real specific IgE was considered as 1,300 UA, showing just how the method of original value >17.5 UA was wrong. This dilution technique was similar to those used for ANA, syphilis and viral antibody titers, which normally showed very high antibody titers in the serum. By this method, the true antibody titers of serum IgE were reported to hospitals for the first time. Later this dilution technique was generally adopted by other laboratories in Japan as well. The results of serum dilution was really amazing: as is shown in the table 1 and Fig. 10, the RAST UA values of Dermatophagoides pteronyssinus (Dp) and Dermatophagoides farinae (Df) were extraordinarily high, compared to many other allergens such as fungi, food, bacteria and pollens.

Table 1: Serum IgE levels of four allergic diseases, demonstrating that atopic dermatitis shows remarkably high levels of IgE compared to other atopic diseases without eczema [1]

Diseases	n (M, F)	IgE (IU/ml)		Age	
		mean	SD	mean	SD
1 Atopic dermatitis	83 (24,59)	2,947.3	5,404.5	23.9	8.3
2 Bronchial asthma	18 (3,15)	336.5	439.8	43.1	22.6
3 Allergic rhinitis	53 (11,42)	323.8	617.1	42.5	17.1
4 Urticaria	54 (20,34)	350.9	678.4	45.5	19.3

Allergens	UA	%
Dermatophagoides pteronyssinus	127	87.0
Fungi (3 types)	5	3.4
Japanese cedar pollen	6	4.1
Food (10 types)	8	5.5
Total	146	100.0



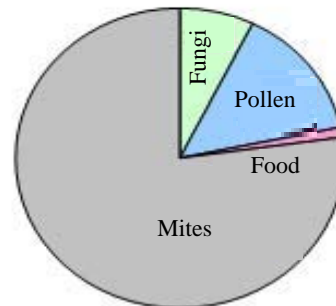
n=42 (17 males and 25 females)

Average age : 23.5 years old

Average serum IgE level : 4,643 IU/ml

In 1991, the serum dilution method was performed on 42 adult AD patients in order to investigate the responsible allergens for serum IgE elevation.

Allergens	UA	%
Dermatophagoides pteronyssinus	340	77.2
Fungi (3 types)	32	7.3
Japanese cedar pollen	63	14.4
Food (10 types)	5	1.1
Total	440	100.0



n=42 (28 males and 14 females)

Average age : 29.8 years old

Average serum IgE level : 6,751 IU/ml

In 2006, the serum dilution method was performed on 42 adult AD patients in order to investigate the responsible allergens for serum IgE elevation.

Fig. 10: (Color)

The rate of causative allergens was calculated using the UA values of RAST among 42 severe cases of atopic dermatitis. 1a is the result obtained in 1991, showing that in average, 87.0% of elevated serum IgE can be attributed to Dermatophagoides. 1b is the result obtained in 2006 among the same number of similar severe cases of atopic dermatitis, showing that in average, 77.2% can also be attributed to Dermatophagoides. Note the increase in the rate of cedar pollens on the production of IgE in 2006, and yet, the responsibility of Dermatophagoides is still very high in the elevated serum IgE with 42 severe atopic dermatitis patients [1].

Such phenomenon were reported for the first time by Okudaira et al in 1983 [17] and 1989 [18], and confirmed by the national research team in 1991 [1] and by Nakayama Dermatology Clinic in Tokyo in 2006 [1]. These already reported tables and figures are again demonstrated to emphasize the importance of them. These results clearly showed that with AD, usually the serum IgE levels were remarkably higher than of other atopic diseases without eczema, and the presence of moderate or severe eczema of AD was highly associated with the rise of serum IgE [1, 2].

For many years, serum IgE had been recognized as a mediator to provoke only type I allergic reactions like allergic rhinitis, bronchial asthma, urticaria and anaphylactic shock. However, in 1986, Bruynzeel Koomen made a great discovery that IgE molecules were present on epidermal Langerhans cells to provoke eczema when causative atopic allergens come into contact from the skin surface [12]. Novak et al confirmed this fact in 2004 and through these discoveries, the link between serum IgE and production of eczema was found [13].

As for the most important causative allergen that produces various atopic diseases, in 1969 Voorhorst et al, also made a great discovery that a type of house dust mite (HDM) called dermatophagoides pteronyssinus (Dp) was responsible in provoking atopic asthma in the Netherlands [14]. They observed that patients with intractable asthma in and around Amsterdam were free of asthma attacks while they stayed in Pyrenees during their summer vacation, and that the asthma came back when they came down from the mountains to hot and humid plains of the lower altitude areas. They examined the house dusts in the plain and in the mountain to discover that there were abundant Dps in the homes in the plain and instead Dps were rare among the houses in the mountain. They made intracutaneous tests of Dps, which were found to be positive among asthma patients. This knowledge gradually prevailed to have shown that HDMs were an important allergen in the houses for the production of atopic asthma.

In 1984, Rawle et al reported for the first time that the P1 antigen of Dps produced a specific positive reaction by the lymphocytes of AD and AD + asthma patients. IgE did not have any relation to this phenomenon. Those lymphocytes of allergic rhinitis and control persons did not react to P1 antigen of Dps [15]. This was the first report of type IV allergy to HDM among AD patients. To ascertain type IV allergy to HDM

in AD, a section of the national research team of AD conceived patch testing's of cultured and crushed live Dps and Dfs placed on slightly convex plastic discs of 8 mm in diameter. It was a device to surely contact fine mite components to the skin for two days as a patch test. The reactions were read on days 2,3 and 7 by ICDRG standards. This test clarified that 12 out of 48 AD patients showed erythema, edema, papules and later eczematiation at the location of the patch test of 3 crushed live mites, a typical type IV positive reaction of allergy. The histopathology of positive patch test reactions to crushed live HDM was spongiosis of the epidermis with infiltration of lymphocytes as ordinary allergic contact dermatitis (Fig. 11). When immunological factors of the inflammation were compared with the original eczema of AD, they were almost identical as is shown in table 2, demonstrating that the eczema of AD and crushed mite allergic patch test reactions were quite similar. It meant that the eczema of AD seemed to be surely produced by the contact of crushed live dermatophagoides. Only 1 crushed mite and crushed dead mites produced negative reactions in all cases [3]. These results showed that type IV allergy, or in another term, contact hypersensitivity to HDM, were surely present among AD patients. Also, when serum IgE level was low and the RAST scores were 0 UA towards common allergens of AD, such cases had been regarded as AD due to intrinsic factors for many years. This is apparently erroneous when patch tests show positive to HDM cases of AD are really present. Imayama et al, a team of national researchers on AD reported that the combination of IgE RAST and patch testing of HDM could be classified for 130 AD patients into four groups: Type I + IV 32 (24.6%), Type I only 42 (32.3%), Type IV only 19 (14.6%), and no allergy to HDM 37 (28.5%) [16]. This was a report that among 130 AD patients, 93 cases (71.5%) were surely allergy to HDM of type I, IV or the both.

Table 2: Results of immunochemical staining of the skin lesions of AD patients and positive mite reactions of the patch tests

	CD4: Helper / Induce T-cell	CD8: Suppressor / cytotoxic T-cell	CD1a: Langerhans cell	ICAM 1	HLA-DR	CD23: Fc ε R2
Eczematous skin lesions of AD patients	11/15 (73.3)	0/15 (0)	8/15 (53.3)	9/16 (56.3)	13/16 (81.3)	1/4 (25.0)
Positive reactions of patch test to Dps or Dfs	13/14 (92.9)	1/14 (7.1)	9/14 (64.3)	13/15 (86.7)	14/14 (100)	2/5 (40.0)

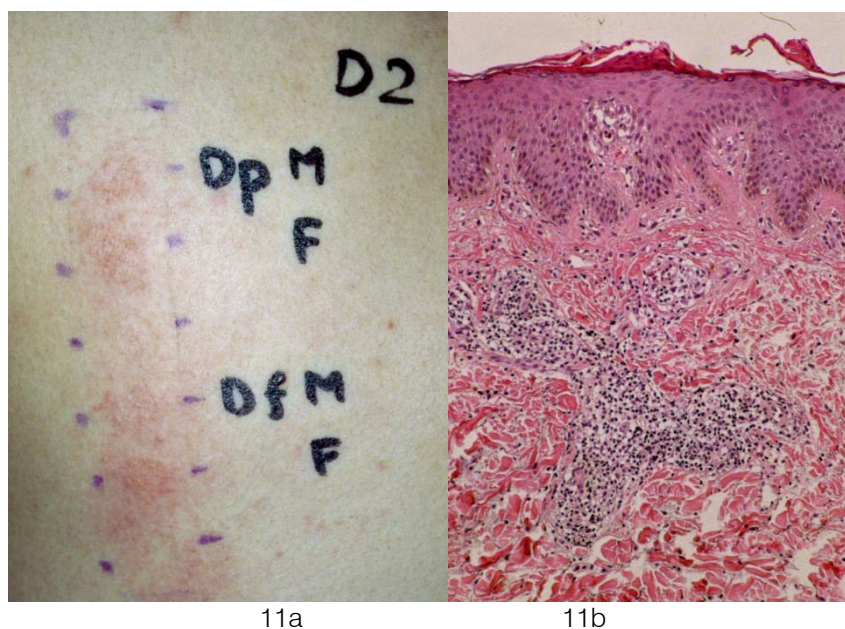


Fig. 11: (Color)

11a: Patch tests of crushed live mites were negative on controls, but showed clear positive eczematous reactions among AD patients, and even on baby AD patients whose serum IgE was normal and the RAST to HDM was negative.

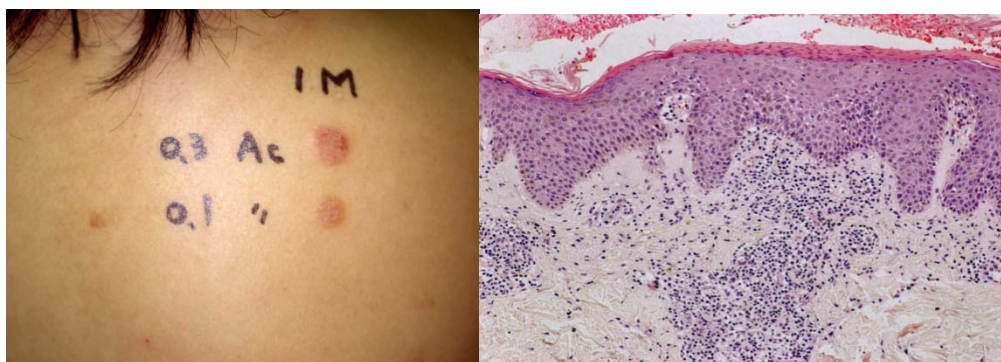
11b: Histopathology of such positive reactions on adult AD patients showed spongiosis and lymphocytic infiltration in the dermis as ordinary allergic contact dermatitis.

Today, such patch testings to find out type IV allergy to HDM is possible by using a Dermatophagoides mix patch test allergen sold by Chemo technique® in Sweden. It was developed by Italian investigators putting a number of Dps and Dfs in petrolatum [17, 18]. One small portion of it should be put on a Finn Chamber to be applied on the back of the patient, and the reactions are examined on days 2, 3 (or 4) and 7 (or 6), as typical allergic positive reactions are frequently seen as late as 3 -7 days. The mistake of diagnosing "intrinsic AD" which occurs without performing mite patch tests can be avoided through this procedure.

Normally, eczematous allergic type IV reactions occur by the contact of allergens having molecules less than 500 KD, like metal ions, hair dyes, fragrances, urushiol, formaldehyde, rubber vulcanizers, woolalcohol etc. Therefore, it was suspected that some chemicals having molecules less than 500 KD must be present in HDM to provoke strong type IV reactions of AD. The procedure of finding out such low molecule contact allergens in HDMs were performed by two groups at the same time.

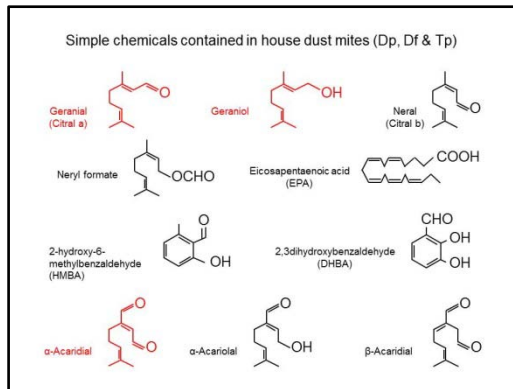
Sakurai et al [19] collected cultured Dps and Dfs on saturated saline water, crushed and extracted terpenes in the HDM by Folch solution, examined by gas chromatography and mass spectrometry. Kuwahara et al cultured HDMs, picked up 40 live mites, put them in hexane and examined them in the same method [20, 21]. Both investigations agreed to have found out

that the richest terpenes in Dps and Dfs were geraniol and geranial. Further more, Kuwahara's group discovered α -acaridial from *Tyrophagus presensitiae* (Tp) through the same method. The chemical structures of these terpenes along with the patch test positive reactions to them are shown in Fig. 12. Geraniol among such terpenes have been known as a common cosmetic sensitizer [23, 24], and the concentrations of geraniol and geranial are insufficient to provoke eczematous reactions from HDM. However, in rare cases, there are inactive AD patients who had not cleaned their room and mattresses for several months. In such cases the amount of terpenes in the room may reach high enough to provoke eczema if they already had such allergens due to cosmetics or toiletries.



12a

12b



12c

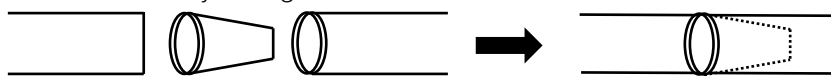
Fig. 12: (Color)

The allergenicity of simple chemicals found in house dust mites detected by patch tests.

The α -acaridial contained in Tp is a primary sensitizer and produced erythema with infiltration for more than a month (12a) and 6 months at the longest when it was patch tested at 0.1% - 0.5% in petrolatum. The histopathology of such long term positive patch test reactions were acanthosis and infiltration in the upper dermis, suggesting that α -acaridial is a causative allergen of Prurigo Besnier of AD. Among 10 terpenes contained in HDM, α -acaridial is the only strong contact

sensitizer (12c). The reason why prurigo is formed when α -acaridial comes into contact is because it cannot be destroyed or eliminated in the dermis to maintain a long term positive allergic reaction. This is much like the case of persistent light reaction due to halogenated salicylanilides.

Visit an AD patient's home with an electric vacuum cleaner (320 W). We recommend driving there with a car instead of using public transport.



1. Insert a small non-woven fabric bag between the tubes to collect HD.
2. Aspirate HD from 1 m² for 20 seconds. (1m² is indicated by a 4m long circular string in the form of a square with 1 m on each side.)
3. Collect HD from 10 – 15 places and medicate each fabric bag with a number.
4. After returning the laboratory, measure the weight of each HD in the bags.
5. Measure 50 mg of HD, put it on a petri dish of 9 cm in diameter. (This kind of petri dish is usually used to culture bacteria in hospitals.)
6. Add 1ml of 0.1% neutral detergent to detach mites from the fragments of house dust.
7. Pour 0.01% methylene blue containing 4ml agar into the petridish after liquidizing it with water at 60 degrees.

8. Pour 0.01% methylene blue containing 4ml agar into the petridish after liquidizing it with water at 60 degrees.



Leave it at room temperature until solid

1. Place a petridish containing MBA under a microscope with a plastic plate with fine parallel lines beneath.
2. Start counting.

On the other hand, α -acaridial turned out to be a primary sensitizer and it proved that it could produce prurigo for months when a patch test was conducted with concentrations of 0.2% - 0.5%. This is the reason why its commercial distribution as a patch test allergen

was refrained, because its distribution was suspect to creating many other new AD patients in the world. However, it should be noted that Tp, a HDM, has such a strong contact sensitizer [1].

III. FOR ACCURATE REDUCTION OF HDM IN THE HOMES OF SEVERE AD PATIENTS, CONDUCT MITE FAUNA INVESTIGATION WITH THE MBA METHOD

For many years, counting the accurate number of HDM in each AD patients' homes had been impossible, because there had not been an excellent

practical method. When three national research teams started to investigate the causation and treatment of intractable AD in 1989, one team developed a practical method of counting the number of mites in every furniture of the patients' homes. This new method, known as the Methylene Blue Agar (MBA) method was easier than the previous methods adopted in acarology. It is shown in Fig. 13, and soon the first laboratory to investigate mite fauna was established in Chiba Prefecture near Tokyo. As HDMs are macroscopically invisible, the invention brought a remarkable progress to evaluate the furniture in the AD patients' homes based on the number of HDM among various locations.

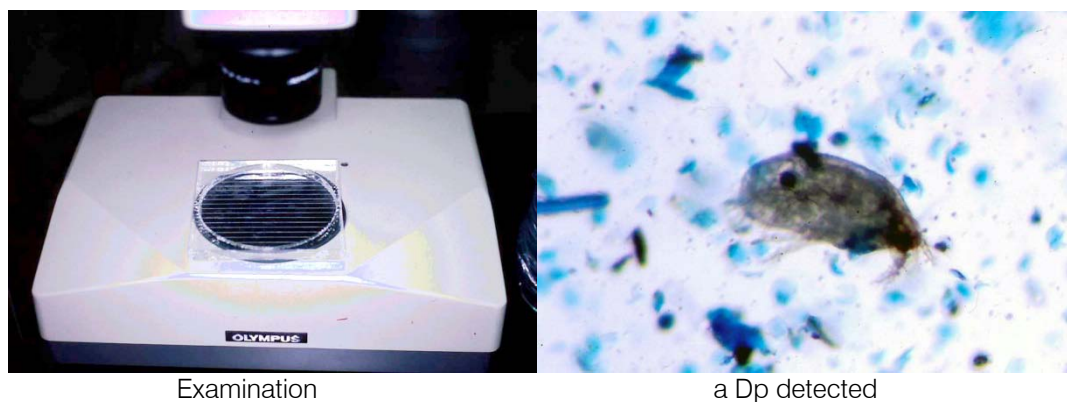


Fig. 13: (Color)

Methylene blue agar (MBA) method to investigate mite fauna

According to the results of crushed live HDM on plastic discs, three or more mites could produce a positive patch test and eczematous reactions. One crushed mite, however, produced no positive reaction at all with the AD patients. When the mite numbers were less than 50/m² per 20 seconds aspiration, it meant the mite number was 1 or 0 in a 10×10 cm area. Therefore, after the mite fauna investigation was conducted, and the patients as well as the doctors were informed of the mite numbers at various locations, the environmental improvement to reduce mite numbers to less than 50 in all places of the home was recommended.

Carpets and tatami, a traditional Japanese straw mat, turned out to be an eminent medium to keep HDM abundant throughout all seasons, therefore, all of

them were advised to be removed, and be replaced with flooring. In cold areas floor heating was recommended to be introduced. Fortunately, the mite-free-sleeping mats had been available at that time, which used high-density cloth produced by Teijin Company through fine woven fibers in which no mite could penetrate into the mat (Fig. 14). All of the intractable AD patients who were hypersensitive to HDM either by type I or IV allergy, were requested to purchase this mite-free-mat, so that they could pass 7 or 8 hours of the night with no contact to HDM at all.

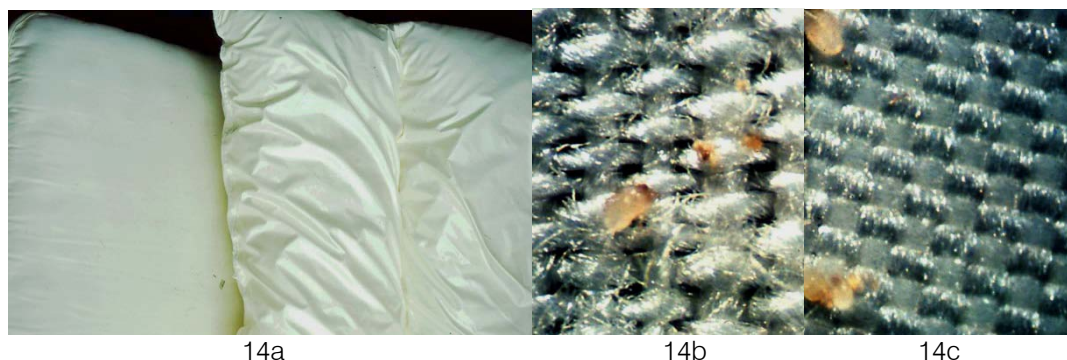
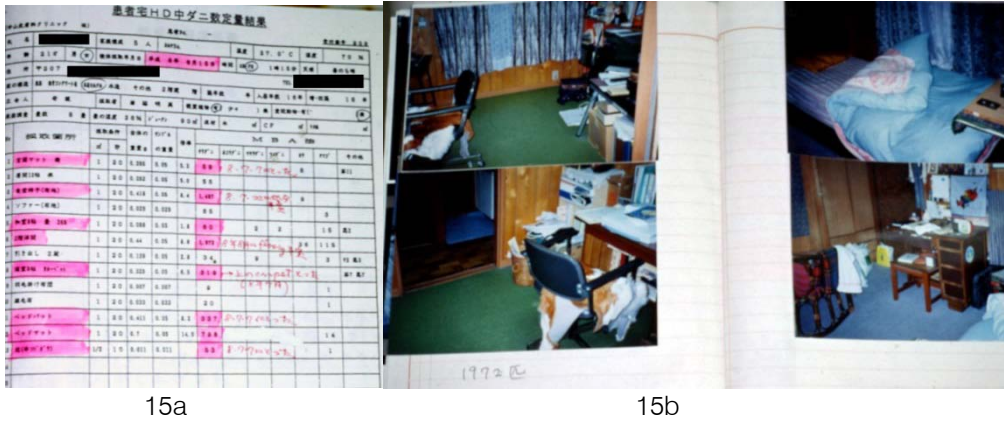


Fig. 14: (Color)

Mite free sleeping mats (14a) are fully protected on the surface by a textile that has no holes for HDMs to enter. This mite-free condition has been realized finally for the first time. Note that ordinary cloths are full of

small holes that make it easy for HDMs (0.3mm) to pass through (14b), but Teijin Co.'s mite-free matt covered with high-density cloth is able to prevent the intrusion of HDMs (14c).



15a

15b



15c

Fig. 15: (Color)

A sample of a report on mite fauna investigation, indicating mite rich furniture in red ink (15a). Using this report, the patient's home condition (15b) was improved to decrease mite numbers to less than 50/m² per 20 seconds aspiration, including the removal of carpets, flooring and the introduction of mite-free-sleeping mats (15c). All the cases in Fig. 1 – 8 had this allergen control treatment to regain normal healthy skin conditions.

Furry chairs and sofas were requested to have the surface replaced with smooth textile which would not allow too much HDM to accumulate. Cleaning the room using a vacuum cleaner once a week was also recommended. Statistics of mite fauna among the number of severe AD patients always showed that 90% of HDM examined were Dps and Dfs, and one example of the study in 1996 is demonstrated in table 3 as well as the distribution of mites in table 4. This ratio has remained basically the same in this century as well [1].

Table 3: Mite species detected from the homes of 140 severe atopic dermatitis patients (MBA Mite Research Laboratory, 1996).

No.	Species	Number	%
1	Dermatophagoides (Dp+Df)	137,348	88.9
2	Tarsonemusae	1,91	1.3
3	Haplochthonius	4,216	2.7
4	Cheyletus	1,151	0.8
5	Others	2,534	1.6
6	Fragments	1,030	0.7
7	Eggs	6,255	4.0
Total		154,465	100.0

The rate of Dermatophagoides (Dp+Df) among HDMs showed between 88% - 93% according to the statistics obtained from 1991 to 2015, showing approximately 90% of HDM had always been Dermatophagoides group. The excellent effect of mite elimination on AD is easy to understand as it means actually the elimination of Dermatophagoides to which severe AD patient are hypersensitive.

Table 4: Average numbers of mites among various furniture in the AD patients' homes during all four seasons in 1993 and 1996. [25]

The number of patients surveyed: 484
(Total number of mites *1 /m² per 20 seconds vacuum aspiration with 320W electric cleaner)

Season		Spring *2	Summer *3	Autumn *4	Winter *5	Total *6
Interior						
1	Carpet (including mat)	144.0 (187)	301.3 (194)	133.3 (122)	98.6 (181)	174.7 (684)
2	Tatami mat (Japanese straw mat)	46.8 (106)	93.4 (153)	53.8 (115)	56.3 (105)	65.4 (479)
3	Flooring	11.5 (102)	55.0 (167)	16.4 (101)	22.5 (112)	30.1 (482)
4	Mattress	17.7 (188)	52.5 (208)	87.1 (163)	42.3 (186)	48.7 (745)
5	Blanket (including towelket)	21.3 (62)	95.5 (97)	112.0 (67)	20.6 (137)	57.6 (363)
6	Floor under tatami mat	236.2 (9)	318.0 (15)	1,289.5 (13)	268.2 (7)	964.4 (44)
7	Mattress of bed	79.5 (40)	98.9 (30)	261.0 (28)	55.2 (34)	116.1 (132)
8	Pillow	4.4 (68)	9.6 (91)	16.1 (63)	9.9 (65)	9.9 (287)
9	Japanese seat cushion	34.0 (21)	41.4 (23)	60.2 (38)	53.9 (19)	49.3 (101)
10	Sofa	219.3 (40)	527.3 (56)	193.2 (40)	798.0 (43)	448.8 (179)
11	Chair	108.3 (23)	377.0 (43)	285.5 (48)	439.3 (28)	314.8 (142)
12	Mite-proof mattress	4.1 (23)	18.8 (50)	7.6 (45)	6.9 (36)	10.5(154)
13	Mite-proof tatami	7.5 (2)	7.3 (4)	13.7 (7)	5.0 (4)	9.4 (17)
14	Mite-proof pillow	0.7 (7)	2.4 (7)	2.3 (12)	0.4 (5)	1.7 (31)
15	Others (ex. Drawer, Closet, etc.)	29.4 (70)	31.2 (116)	28.9 (112)	37.8 (95)	31.8 (393)

*1 Counted by the MBA method, except for in the case of insects, the egg and mite shell were counted as one. The figure in () is a sample.

*2 March - May *3June - August *4September - November *5December– February

*3 January - December

IV. THE RESULTS OF MITE REDUCTION BASED ON MITE FAUNA INVESTIGATION

House dust mites are invisible and even though hundreds or thousands of them swarm in furniture, they make no noise, and therefore their presence are not recognized by the inhabitants who suffer from years of severe, generalized itchy eczema. The recognition that HDMs are the critical main causation of severe, intractable AD patients, has been proven by the accumulated evidence from years of research [1, 2]. These patients long for a real cure like the AD cases presented in Fig. 1 to 8 of this article. Such a cure is surely possible if the patients are examined with serum IgE level, RAST on Dp, Df, Tp and other allergens related to AD, a patch test using HDM and other common contact sensitizers related to contact dermatitis. When the patients turn out to be hypersensitive to HDM, mite fauna should be investigated by visiting the patients' homes and investigating the mite number of each furniture.

Environmental improvement should be recommended in order to reduce mite numbers in all areas of the home to less than 50/m² per 20 seconds aspiration because it is a lower threshold that does not provoke eczematous or prurigo-type skin reactions.

When a national research team investigated in 1995, 15 out of 17 severe AD cases (88%) recovered

and kept well improved conditions in the same season for one of two years after, as they could execute the above mentioned reduction of HDMs (complete group). On the other hand only, 6 out of another 17 similar AD cases (35%) were still able to recover even when some mite rich furniture were kept as before (incomplete group). This was a double-blind test, and there was a significant statistical difference between the complete group and incomplete group when examined by the Wilcoxon test [1, 2, and 25].

In following years, Tan performed similar double blind tests by measuring the HDM population with antigen. The results were similar in which when the mite reduction was incomplete, the result of improvement also decreased [26]. After these DBT, a simple follow up of mite reduction on intractable severe AD have been made. Two reports were made on the effect of mite elimination with color photographs like Fig. 1 – 8 of this paper after mite-free mattresses had been used by the severe AD patients [27, 28]. Such mite free mattresses should be produced and distributed using high density textile (Microguard®) because pesticide is quite unnecessary in creating mite free conditions at night.

As doctors are always busy, a person who is informed of the address and map of the patient's home should make a visit after an appointment is made. A 320W vacuum cleaner with 10 – 20 non-woven fabric bags should be inserted between the tubes to collect

house dusts. One room in the laboratory or the hospital is enough to perform the MBA method mite fauna investigation, if petri dishes, water bath, MBA, stereotypical microscope and a plastic disc with parallel lines on it to avoid double count are all ready. In Japan the cost of mite fauna investigation is about 340 USD plus transportation fee. The report is delivered to the clinic two weeks after the visit.

V. CONCLUSION

Thus, dermatologists should be courageous enough to recommend a mite fauna investigation followed by mite reduction to less than 50/m² per 20 seconds aspiration in all areas of the AD patient's home, if they encounter a patient with generalized itchy eczema that could not be improved through anti symptomatic treatments. When mite reduction is incomplete, you cannot anticipate for good results. For this purpose, mite fauna investigation using MBA method and the production and distribution of mite-free mattress should be available in all countries where there are many AD patients. Without these, AD is considered to be incurable among many severe intractable cases. We should not consider that the causation of severe, intractable AD is unknown, and understand that AD is curable when the causation of mite allergy is detected either by IgE-RAST or patch testing using adermatophagoides mix.

Establishing a laboratory to perform MBA method investigation and the production and distribution of reliable mite-free mattresses using high density textile (Teijin) are certainly a barrier at present, but the barriers are not high, since they have been available in Japan for more than 20 years. Furthermore severe and intractable AD patients should be taught that HDMS, the invisible and silent creatures which share one's home, are most important causation of their recurrent itchy dermatoses. The investigation of mite fauna followed by scientific reduction to less than 50/m² per 20 seconds aspiration can cure the disease for many years.

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