Further studies are needed to shed light on the biological reasons for these findings.

The authors are indebted to Dr Denise Ponard for C1Inh analyses and for helpful discussions.

Ludovic Martin, MD, PhD[a,b]
Nadia Raison-Peyron, MD[b,c]
Markus M. Nöthen, MD[d,e]
Sven Cichon, PhD[d,e]
Christian Drouet, PhD[b,f]

From [a]the Department of Dermatology, Orléans Hospital, France; [b]the French Reference Center for Angioedema, Grenoble, France; [c]the Department of Dermatology, Montpellier University Hospital, France; [d]the Department of Genomics, Life and Brain Center, and [e]the Institute of Human Genetics, University of Bonn, Germany; and [f]Joseph-Fourier University, Centre National pour la Recherche Scientifique, Unité Mixte de Recherche 5525, Grenoble, France. E-mail: ludovic.martin@chr-orleans.fr.

Disclosure of potential conflict of interest: The authors have declared that they have no conflict of interest.

REFERENCES

1. Agostoni A, Aygoren-Pursun E, Binkley KE, Blanch A, Bork K, Bouillet L, et al. Hereditary and acquired angioedema: problems and progress: proceedings of the Third C1 Esterase Inhibitor Deficiency Workshop and beyond. J Allergy Clin Immunol 2004;114:S51-131.
2. Bork K, Barnstedt SE, Koch P, Traupe H. Hereditary angioedema with normal C1-inhibitor activity in women. Lancet 2000;356:213-7.
3. Binkley KE, Davis A. Clinical, biochemical, and genetic characterization of a novel estrogen-dependent inherited form of angioedema. J Allergy Clin Immunol 2000;106:546-50.
4. Martin L, Degenne D, Toutain A, Ponard D, Watier H. Hereditary angioedema type 3: an additional French pedigree with autosomal dominant transmission. J Allergy Clin Immunol 2001;107:747-8.
5. Cichon S, Martin L, Hennies HC, Müller F, van Driesche K, Karpushova A, et al. Increased activity of coagulation factor XII (Hageman factor) causes hereditary angioedema type III. Am J Hum Genet 2006;79:1098-104.
6. Farsetti A, Misiti S, Citarella F, Felici A, Andreoli M, Fantoni A, et al. Molecular basis of estrogen regulation of the Hageman factor XII gene expression. Endocrinology 1995;136:5076-83.
7. Cicardi M, Bergamaschini L, Zingale LC, Gioffré D, Agostoni A. Idiopathic nonhistaminergic angioedema. Am J Med 1999;106:650-4.
8. Cicardi M, Zingale L. Clinical manifestations of HAE. J Allergy Clin Immunol 2004;114:S55-61.
9. Drouet C, Blanch A, Roche O, Monnier N, Duponchel C, Kalmar L, et al. HAE: genetic investigations. J Allergy Clin Immunol 2004;114:S65-74.
10. Bork K, Gül D, Dewald G. Hereditary angioedema with normal C1-inhibitor in a family with affected women and men. Br J Dermatol 2005;154:542-5.
11. Gupta S, Yu F, Klaustermeyer WB. New variant hereditary angioedema in three brothers with normal C1 esterase inhibitor level and function. Allergy 2004;59:557-8.

Available online September 10, 2007.
doi:10.1016/j.jaci.2007.07.002

Nonwoven in contrast to woven mattress encasings accumulate mite and cat allergen

To the Editor:

Sensitivity to indoor allergens, including house dust mites, is common in patients with asthma, and national guidelines recommend decreasing indoor allergen exposure in such patients.[1] Measures to decrease mite allergen exposure have been extensively studied and reviewed,[2] but controversy exists about the effectiveness of particular measures. Beds are a major source of mite allergen. It is clear that if avoidance measures are to be successful at decreasing symptoms, they must succeed in reducing allergen exposure.[3,4]

Allergen-proof encasings can be made from vinyl or from laminates of impermeable or semipermeable membranes, but most current encasings are constructed from microfiber barrier fabrics. These allow air and water vapor transmission but have pore sizes small enough to block the passage of allergen.

There are 2 classes of allergen-impermeable, air-permeable barrier fabrics: woven and nonwoven. Woven fabrics are made from long yarns woven horizontally and vertically to create the barrier fabric. Woven fabrics can be washed repeatedly without losing their integrity, and those with a pore size of 6 μm or less are able to block the passage of mite and cat dander allergens.[5] Nonwoven barrier fabrics are made from short lengths of filaments compressed and bonded together into a solid mass, much like felt, and have something of the look and feel of a thick paper towel. Nonwoven encasings are less expensive than woven encasings, but they are generally less durable and in some cases should not be washed. Although they are tight enough to block the passage of allergen in short-term experiments,[5] recent studies have suggested that nonwoven encasings are of sufficient depth to allow dust mite penetration and occasional colonization.[6,7] This depth could possibly also be sufficient to accumulate allergen, which would in turn negate the benefit of the fabric as an allergen barrier.

To investigate this, we carried out 2 studies: (1) examination of live mites and mite feces placed on the surface of these fabrics and (2) assay of allergen levels on mattress encasings that had been in daily use for more than 1 year.

Microscopic observation of cultured *Dermatophagoides pteronyssinus* mites placed on the woven microfiber encasing confirmed that the mites cannot penetrate into the fabric (see Fig E1, *A* [video], in this article's Online Repository at www.jacionline.org), with no penetrations seen during a 1-hour period of observation. Conversely, many of the mites placed on the nonwoven encasing burrowed beneath the filaments of the fabric, some within seconds (see Fig E1, *B* [video], in this article's Online Repository at www.jacionline.org). Sieved pure mite feces placed on the surface of the woven encasings could be easily wiped off (see Fig E2, *A* [video], in this article's Online Repository at www.jacionline.org). In contrast, with nonwoven encasings, attempts at wiping pushed the majority of fecal particles into the substrate of the encasing (see Fig E2, *B* [video], in this article's Online Repository at www.jacionline.org).

To investigate whether allergen accumulated on the surface of these encasings during normal use, we obtained 20 nonwoven mattress encasings and 12 woven mattress encasings (of the same types as shown in Figs E1 and E2 in this article's Online Repository at www.jacionline.org)

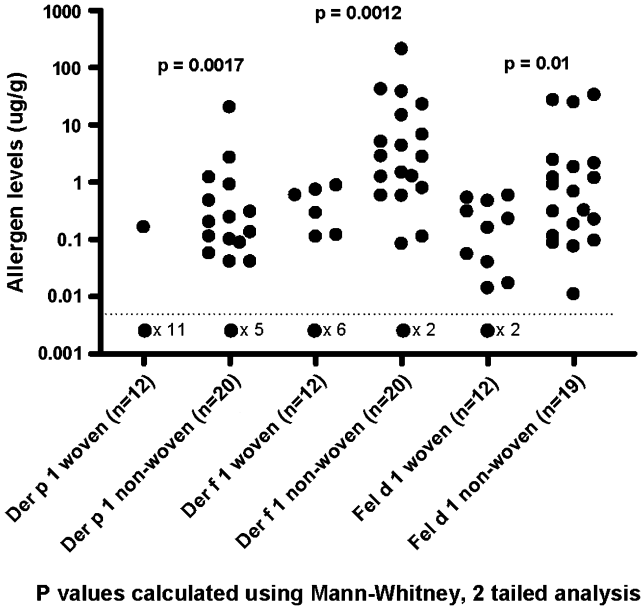


FIG 1. Concentration of mite and cat allergens in dust from the outside of mattress covers that had been in regular use for approximately 17 months. *P* values were calculated by using the Mann-Whitney *U* test, 2-tailed analysis.

from patients who had used them continuously for at least 1 year (mean period of use, 17.2 months and 17.5 months, respectively). The nonwoven and woven fabrics used in these encasings had been demonstrated to be impermeable to Der p 1 and Fel d 1 by using the technique described previously.[5] Mattress covers were returned by express mail and kept at 75% relative humidity for several days before they were examined for live mites. They were then refrigerated for up to 2 weeks before collection of dust samples and assays of allergen levels (see Table E1 in this article's Online Repository at www.jacionline.org for details of dust collection and assays).[8]

A 15 × 15–cm area at the head end of the top outer surface of each mattress encasing was first examined microscopically for mite colonization and then checked for live mites by using the heat escape method.[9] With this technique, gradually increasing heat causes any live mites to move upward to a clear adhesive paper placed on the fabric, where they can be counted. Subsequently, dust samples were obtained from a square meter of the outer and inner surfaces of each used encasing by vacuuming. These samples were weighed and analyzed for Der p 1, Der f 1, and Fel d 1 by means of ELISA (see Fig 1 and Fig E3 and Table E1 in this article's Online Repository at www.jacionline.org).[8]

Four of the used nonwoven encasings had macroscopically visible dirt and dust embedded in their fabric. Although no mites were seen either by means of microscopy or heat escape, the used nonwoven encasings had higher quantities of dust and higher levels of mite allergen on their outer surfaces (see Fig 1 and Table E2 in this article's Online Repository at www.jacionline.org), with mean Der p 1 and Der f 1 concentrations of 1.35 μg/g and 17.74 μg/g, respectively, compared with mean concentrations of 0.014 μg/g and 0.227 μg/g, respectively, on the used woven encasings ($P < .001$, Mann-Whitney *U* test). Nine of 20 nonwoven mattress encasings had levels of Der p 1, Der f 1, or both of greater than 2 μg/g on their outside surface, and 5 had levels of greater than 10 μg/g. High levels of Fel d 1 were also present on the outer surface of 5 of 20 used nonwoven mattress encasings, but none of the 12 used woven encasings, despite the fact that at least 2 of the owners of the woven encasings allowed a cat in the bedroom. Mean Fel d 1 was 5.1 μg/g on the nonwoven encasings and 0.2 μg/g on the woven encasings ($P = .01$). Comparable differences in mite and cat allergen were found in dust samples from the inside of the fabrics (see Table E2 and Fig E3 in this article's Online Repository at www.jacionline.org).

Taken together, these findings indicate that the ability of a fabric to block the passage of allergen over a 20-minute period is by itself an insufficient criterion for its use in allergen avoidance. The encasing should also be smooth enough to prevent mite colonization and to prevent allergen accumulation. Because we were unable to find mites in the encasing material itself, it is not clear that the mite allergen measured on its surface was produced by mites that had colonized the fabric. More likely, the nonwoven fabric, with its irregularly shaped interstices, was acting as a sink that trapped and retained allergen produced elsewhere. This is supported by the high cat allergen levels and the video imaging showing mite fecal entrapment in the nonwoven fabric. We cannot exclude, however, the possibility that some of the mite allergen was

produced by mites that had colonized the fabric but left that substrate before it was studied.

The finding of high allergen levels and the fact that mites can penetrate into these fabrics raise serious questions about the use of nonwoven fabrics for allergen avoidance.

Jeffrey D. Miller, MD[a]
Lisa Naccara, BA[b]
Shama Satinover, MS[b]
Thomas A. E. Platts-Mills, MD, PhD[b]

From [a]Allergy and Asthma Associates, Danbury, Conn, and [b]the University of Virginia Health Sciences Center, Charlottesville, Va. E-mail: JeffreyMillerMD@comcast.net.

Funded by Mission: Allergy, Inc, and National Institutes of Health grant AI-20565.

Disclosure of potential conflict of interest: J. D. Miller owns stock in and is employed by Mission: Allergy, Inc. T. A. E. Platts-Mills has consulting arrangements with Indoor Biotech and has received grant support from the National Institutes of Health. The rest of the authors have declared that they have no conflict of interest.

REFERENCES

1. National Asthma Education and Prevention Program Expert Panel Report. Guidelines for the diagnosis and management of asthma. Bethesda (MD): National Institutes of Health; 1997. Publication no. 97-4051.
2. Arlian LG, Platts-Mills TAE. The biology of dust mites and the remediation of mite allergens in allergic disease. J Allergy Clin Immunol 2001; 107(suppl):S406-13.
3. Platts-Mills TAE. Allergen avoidance. J Allergy Clin Immunol 2004;113: 388-91.
4. Gøtzsche PC, Johansen HK, Schmidt LM, Burr ML. House dust mite control measures for asthma. Cochrane Database of Syst Rev 2004;4: CD001187.
5. Vaughan JW, McLaughlin TE, Perzanowski MS, Platts-Mills TA. Evaluation of materials used for bedding encasement: effect of pore size in blocking cat and dust mite allergen. J Allergy Clin Immunol 1999;103: 227-31.
6. Mahakittikun V, Jirapongsananuruk O, Nochot H, Boitano JJ, Tungtrongchitr A. Woven material for bed encasement prevents mite penetration. J Allergy Clin Immunol 2003;112:1239-418.
7. Mahakittikun V, Boitano JJ, Tovey E, Bunnag C, Ninsanit P, Matsumoto T, et al. Mite penetration of different types of material claimed as mite proof by the Siriraj chamber method. J Allergy Clin Immunol 2006;118:1164-8.
8. Woodfolk JA, Hayden ML, Miller JD, Rose G, Chapman MD, Platts-Mills TAE. Chemical treatment of carpets to reduce allergen: a detailed study of the effects of tannic acid on indoor allergens. J Allergy Clin Immunol 1994;94:19-26.
9. Bischoff ERC, Fischer A, Liebenberg B. Assessment of mite numbers: new methods and results. Exp Appl Acarol 1992;16:1-14.

Available online September 13, 2007.
doi:10.1016/j.jaci.2007.06.048

Successful treatment of 3 patients with recurrent idiopathic angioedema with omalizumab

To the Editor:

Omalizumab is a recombinant humanized monoclonal anti-IgE antibody that is US Food and Drug Administration–approved for the treatment of moderate-to-severe persistent asthma.[1] Omalizumab also has demonstrable effects on inflammation in other conditions.[2-5] We report 3 cases of refractory idiopathic angioedema that resolved on treatment with omalizumab.

Before instituting omalizumab, each patient had undergone aggressive medical management of idiopathic angioedema. Interventions included cessation of medications or foods associated with angioedema. Patients also had to demonstrate failure to respond to (patient 3) or tolerate tapering and cessation of (patients 1 and 2) systemic corticosteroids, despite pharmacologic interventions, including H1 and H2 blockade.[6]

Patient 1 is a 65-year-old white man with a history of moderate persistent asthma and sarcoidosis who had recurrent angioedema in 1999. He experienced swelling in his feet, scrotum, face, tongue, and larynx approximately twice weekly. These attacks required self-administered epinephrine and emergency department visits, hospitalizations, or both about twice monthly. The patient attributed his angioedema to certain foods, but dietary restriction of beef, peanuts, coffee, eggs, and chocolate was not beneficial. Angioedema recurred despite cessation of lisinopril, ibuprofen, aspirin, and allopurinol. Urticaria was absent. Physical examination was unremarkable. Laboratory findings included normal values for complete blood count (CBC) with differential, comprehensive metabolic panel, antinuclear antibody, and thyroid-stimulating hormone; C2 level of 2.1 mg/dL (1.6-4.0 mg/dL); C4 level of 30 mg/dL (16-47 mg/dL); C1 inhibitor level of 37 mg/dL (21-39 mg/dL); normal C1 inhibitor function; C1q level of 16.2 mg/dL (11.8-23.8 mg/dL); positive RAST result to coffee (class 0/1), egg white (class 2), and beef (class 3); and total IgE level of 244 kU/L (0-144 kU/L). In November 2005, 300 mg of subcutaneously administered omalizumab every 3 weeks was instituted for treatment of his asthma. Soon after omalizumab was initiated, the patient's angioedema regressed. He currently remains asymptomatic.

Patient 2 is a 63-year-old white man with a history of chronic obstructive pulmonary disease who had angioedema of his tongue and face in 2003. He denied any urticaria or pruritis with the angioedema. Angioedema remitted for 3 years; he then began having recurrent episodes of lip, tongue, and laryngeal edema, requiring 8 emergency department visits and a hospital admission. The patient required prolonged courses of oral steroids in addition to daily fexofenadine, cetirizine, and ranitidine. Angioedema episodes persisted, despite cessation of lisinopril and ibuprofen. The patient stated that his angioedema occasionally occurred after ingestion of shellfish, tuna, pineapple, chocolate, or coconut, but elimination of these foods did not alleviate the recurrent angioedema. Physical examination was unremarkable. Laboratory findings included the following: normal values for CBC with differential and comprehensive metabolic panel; negative results for anti-FcεRI; low thyroid-stimulating hormone value of 0.031 mIU/L (0.4-4.0 mIU/L) but normal free T4 and total T3 levels, no abnormal antithyroid peroxidase and antithyroglobulin antibody titers, and reduced thyroid radionuclide iodine uptake (4.2%), with slight diffuse gland enlargement; C2 level of 3.4 mg/dL (1.6-4.0 mg/dL); C4 level of 25 mg/dL (16-47 mg/dl); normal C1 inhibitor level and function; total

TABLE E1. Summary of dust sample sieved from encasings (in milligrams) and the concentration of allergen measured within the extracted dust

	Woven (n = 12)		Nonwoven (n = 20)	
	Outside	**Inside**	**Outside**	**Inside**
Dust collected* (mg)				
Mean	47.0	61.9	265.7	210.3
Geometric mean	31.19	35.4	138.1	116.6
Range	12-137	5-250	20-1400	50-1000
Allergen measured† (ng/mL)				
Der p 1				
Mean	1.17	2.51	77.2	64.5
Geometric mean	15.2	3.58	10.3	13.3
Range	0-15.2	0-20.3	0-1020	0-920
Der f 1				
Mean	10.1	40.9	990	1368
Geometric mean	10.4	14.0	87.3	48.0
Range	0-52.8	0-379	0-11400	0-20900
Fel d 1				
Mean	6.17	4.49	55.6	107.4
Geometric mean	4.28	2.52	9.89	19.5
Range	0-22.3	0-24.8	1.07-438	0-662

*Dust samples were collected with a handheld vacuum cleaner—a Hoover Turbo Power 1000 (Hoover, Glenwillow, Ohio)—by using an attachment to collect dust onto a cloth. Vacuum cleaning was carried out over 1 m^2 for 4 minutes. Dust samples were sieved through a 300-μm pore size filter, and the sieved dust was weighed and extracted in borate-buffered saline at 4°C overnight. After removing dust by means of centrifugation, extracts were stored at −20°C.
†Assays to measure allergens by using paired mAbs and standards were carried out as described in detail elsewhere.[8]

TABLE E2. Summary of values for allergen

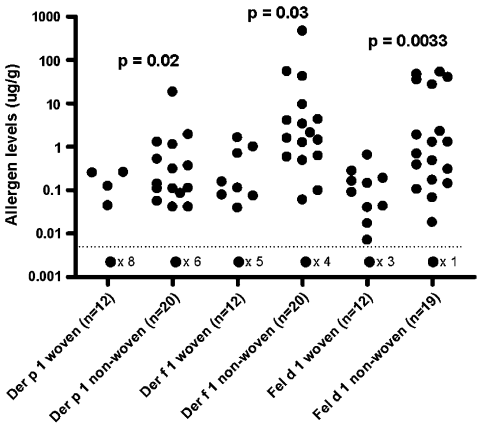
Mattress encasings	Der p 1 concentration (μg/g)		Der f 1 concentration (μg/g)		Fel d 1 concentration (μg/g)	
	Outside	Inside	Outside	Inside	Outside	Inside
Woven						
Range	0-0.163	0-0.260	0-0.873	0-1.632	0-0.584	0-0.647
Mean	0.01	0.06	0.23	0.32	0.20	0.13
SD	0.05	0.10	0.32	0.52	0.22	0.18
Median	<0.01	<0.01	0.056	0.076	0.108	0.067
25% to 75%	0-0	0-0.8	0-0.44	0-0.43	0.02-0.39	0.01-0.18
Geometric mean*	0.163‡	0.26†	0.337‡	0.215†	0.125†	0.082‡
95% CI	0-0	0.0036-0.34	0.0024-0.10	0-1.02	0.08-0.40	0.025-0.30
Nonwoven						
Range	0-20.4	0-18.4	0-210	0-466	0.011-33.4	0-53.00
Mean	1.35	1.23	17.77	29.60	5.10	11.11
SD	4.53	4.07	46.93	103.75	10.49	18.63
Median	0.107	0.109	2.115	1.344	0.798	0.984
25% to 75%	0.02-0.40	0.02-0.44	0.58-10.7	0.08-4.17	0.11-2.12	0.14-27.0
Geometric mean*	0.281‡	0.277†	3.11‡	2.57†	0.675†	1.28‡
95% CI	0-5.68	0-4.23	0.05-0.36	0-0.84	0.05-10.7	2.30-21.2

These data are also shown in Fig 1 and Fig E3.

*Geometric mean values calculated on the positive values.

†$P < .05$, woven versus nonwoven, Mann-Whitney U test, 2-tailed analysis.

‡$P < .01$, woven versus nonwoven, Mann-Whitney U test, 2-tailed analysis.



P values calculated using Mann-Whitney, 2 tailed analysis

FIG E3. Concentration of mite and cat allergens in dust from the inside of mattress covers that had been in regular use for approximately 17 months.