

Research and Innovation on House Dust Mites

Vanna Mahakittikun, M.D., John J. Boitano

The Siriraj Dust Mite Center for Services and Research, Department of Parasitology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

Siriraj Med J 2010;62:90-92

E-journal: <http://www.sirirajmedj.com>

Allergic diseases caused by house dust mites (HDMs) are most important and have the highest prevalence among other types of allergic diseases. In the past 40 years, there have been numerous epidemiological surveys^{1,2} and studies involving in-vivo skin prick testing^{3,4} in Thailand dealing with mite-related diseases. These have indicated that the species, *Dermatophagoides pteronyssinus* and *D. farinae* were, and are, the most important allergens producing allergic disorders in Thais, with cockroaches a distant second.⁵⁻⁷ These realizations generated a plethora of gap-filling, comprehensive investigations dealing with the ubiquitous house dust mite in such diverse areas as vaccine prophylaxis, immunological mechanisms, acarological identification, dust allergies/atopy, mite/allergen avoidance procedures, etc.

The followings are mile stones of our research which has resulted in publications and produced methodological innovations dealing with dust mites. There are three broad areas, which including services, research and education.

In 1997, research dealing with HDMs started in the Department of Parasitology, Faculty of Medicine Siriraj Hospital, Mahidol University with a small cup of dust mite cultures for teaching purposes. Three year later, this modest development was expanded to include mass production for both research and commercial purposes. However, the equipment was lacking for such an enterprise, so we had to invent our own apparatus and techniques specifically given over to large scale production. This resulted in the establishment of new innovations and intellectual properties for the production of purified dust mites. These developments were presented at the World Allergy Congress, in Vancouver, Canada, in 2003.⁸

The intellectual properties associated with these advances included a "Mite isolator" (Patent number 23451) for the separation of mites from their culture media, detailed under the "Method for Mite Purification" (Trade Secrets number 3256). The "MU-Siriraj Mite Feed Formula" and the "Mite culture media dispenser" (Petty patent number 1435) for distributing mite food into containers was also promulgated at this time, along with extraction procedures for an in-house mite vaccine.⁹ Presently it is possible to produce highly puri-

fied dust mites (99% pure mites) for both molecular research and as a source for the Siriraj Mite Vaccine Project (SMAV). Recently an agreement was signed with the Greater Pharma company (Thailand), thereby enabling commercial production of the mite vaccine. In comparison, Thailand is the second amongst four countries producing pure mites for vaccine production. The first is Allergon (Sweden) which was selling at 2,000 USD/gm.

Since allergic diseases have high prevalence in almost every country in the world, products claiming to be mite-proof or anti-mite are of great interest to the general public. However, the caveat here is that many of these product lack scientific validation to support their assertions of hypoallergenicity and the avoidance of both live mites and their allergens with a concomitant relief of suffering. There has been little information to support, and not enough to answer many of the following questions, such as: how to make beddings that are free from dust mites; how fast do mite allergens accumulate in the environment; how to assess the efficacy of anti-mite covers; and in general, what is the mechanism of the available anti-mite products in the market affording consumer protection. All these queries need scientific research in order to secure a knowledgeable and educated public.

In response to inquiries from patients and non-patients alike, the dust mite team concentrated on ways to control both dust mites and their allergens, thereby reducing exposure. Therefore, in 2001, the "House Dust Mites and Allergic Diseases Research Project" was established by Assoc. Prof. Vanna Mahakittikun, Prof. Chaweewan Bunnag and Prof. John J. Boitano (USA). It was housed in the Department of Parasitology located on the 7th floor of the Adulayadejvikom building, Siriraj Hospital. The initial objectives not only focused on a large scale production of dust mites for researchers at the National University of Singapore, but also for research mainly on the control of dust mites. Later, in 2007, the project became known as the "Siriraj Dust Mite Center for Services and Research" (SDMC), and has continued under that name until the present.

In 2000, Assoc. Prof. Vanna Mahakittikun et al., began research on the control of house dust mites in response to frequently asked questions on how to get

rid of dust mites and their allergens. The first paper published in the *Allergy Journal* in 2000 was research that dealt with the optimum temperature for killing dust mites.¹⁰ It was found that the thermal death point was 55°C.

In 2001, Assoc. Prof. Vanna Mahakittikun became interested in the protective mechanism of anti-mite covers against dust mites. The first study on anti-mite covers was published in a Thai local journal "Siriraj Medical Gazette" under the title "Cloth can protect against house dust mite".¹¹ It was the impetus to explore further because there were few papers dealing with the specific materials used for anti-mite covers¹²⁻¹³. The resultant study was published in the *Allergy Journal* (Impact factor 3.161) entitled the "Laboratory assessment of the efficiency of encasing materials against house dust mite and their allergens".¹⁴ The objective was to investigate the efficiency of different encasements against house dust mites and their allergens, in vitro. Four types of materials were evaluated including; a plastic cover, polyurethane coated covers, non-woven covers, tightly woven microfiber covers and a regular cotton bed sheet (as a control). This study was one of the first utilizing our own laboratory assessments for testing the efficacy of the covers by the Heat Escape method, the Siriraj Chamber method and an enzyme-linked immunosorbent assay (ELISA). It was found that the three assessment methods could effectively evaluate the quality of covering materials for in vitro testing, and emphasized, as key factors, pore size and whether mites could colonize within the fabric texture.

These outcomes were not only published in high quality journals of the world, but also led to the introduction of our new innovation, a mite cage¹⁵ called the "Siriraj Chamber" (Patent number 21441). Its usefulness resided in not only testing fabrics for mite penetration, but also for the biological study of the lifecycle of house dust mites. Two additional publications¹⁶⁻¹⁷ soon appeared in journals with higher impact factors; the *Journal of Allergy and Clinical Immunology*; first as a Letter to Editor entitled "Woven Material for Bed Encasement Prevents Mite Penetration" and the original paper, "Mite penetration of different types of material claimed as mite proof by the Siriraj chamber method". (JACI impact factor 6.831, 8.829 respectively). The latter research attracted great interest from the Thailand Textile Institute (ThTI), which culminated in a signing of a Memorandum of Understanding (MOU) between Mahidol University and ThTI. The formal agreement in Sept. 2005 signified a cooperative venture between the testing of mite/allergen penetration of different fabrics in Mahidol University and the testing of the physical characteristics (air permeability, thread count, weft, etc) of these same fabrics at ThTI. In addition, financial support was also extended. A collaboration with the American Association of Textile, Chemist and Colorist (AATCC) for the short- and long-term assessment of the anti-house dust mite properties of textiles occurred shortly thereafter, and was followed by the Pre-Clinical Award on "Assessment on Anti-mite covers" from the Faculty of Medicine Siriraj Hospital in 2007.

Concomitant with these developments was a rapidly expanding clientele who were desirous of having their products tested for a variety of reasons, as mite/allergen penetration, anti-mite solutions on fabrics, the effectiveness of aerosol sprays, the efficacy of an air

sterilizer on eradicating live mites and their allergens, and even aliquots of dust. All of these services to the general public were revenue-producing.

Between 2005 and 2007, a flurry of activity occupied the mite team. Fabrics had been collected by colleagues from different countries and were analyzed for mite/allergen penetrability. Manuscripts were prepared for both local and international presentations, and submitted for publication. Dust mite workshops continued. Educational materials were produced.

Meanwhile other groups of researchers were also interested in studying further aspects of house dust mites; e.g. Assoc. Prof. Sirirchit Wongkamchai focused on chemical agents for killing mites¹⁸ and applied these acaricides to clothing. Her study "the efficacy of various synthetic pyrethroid-impregnated encasement materials against house dust mite under laboratory conditions" was published in *Experimental and Applied Acarology*.¹⁹

Fellows in the Department of Pediatrics studied "House Dust Mite Allergens Accumulate More Rapidly in Synthetic and Kapok Mattresses than in Coconut and Sponge Mattresses" which was presented at the American Academy of Allergy, Asthma & Immunology Conference, held in New York, USA in 2002.²⁰ These results revealed that the studied mattresses could harbor dust mite fauna, in which their allergens would reach significant levels after four months of use.

The usefulness of Thailand's medicinal plants in eradicating mites was also studied by Assoc. Prof. Noppamas Soonthornchareonnon who isolated an important acaricidal activity and formulated it into a herbal extract.²¹⁻²² It was subsequently registered as Trade Secret number 5214.

When the World Allergy Congress (WAC) was awarded to Mahidol University in 2007, Prof. Pakit Vichayanond; the President of the Allergy and Immunology Society of Thailand suggested the possibility of hosting a dust mite workshop. The Department of Parasitology recruited three outstanding researchers in the dust mite field as guest speakers; viz. Prof. Thomas Platts-Mills (HDM, the Most Important Allergen) from the United States, and from Australia, both Dr. Wayne Thomas (Trends in Mite Allergen Research) and Dr. Euan Tovey (the Control of HDMs). The lab practicums were equally successful and featured: (a) under Biology, live mites viewed through a stereomicroscope and hands-on preparation of mite slides; (b) Dust Analyses for immunological diagnosis; (c) Tests for the detection of Mite Allergens; (d) Physical Methods for the Control of HDMs; and (e) Anti-mite covers and agents. The center piece of the laboratory display area was a large 4-poster bed with small to large sized replica dust mites on it. Never before had such a workshop been offered at a meeting of the WAC. There were 75 participants from 34 countries around the world registered for the workshop. This experience served as a template for our own workshops, which have been offered yearly up until the present time. These courses aimed to (i) provide training in the theoretical and practical aspects of house dust mites, and cover [a] the science of HDMs, [b] how HDMs contribute to the development of allergies, [c] mite allergen measurements, [d] efforts to control HDMs and [e] available anti-mite products; (ii) equip trainees with specialized skills for potential research with HDMs; and (iii) communicate our research on the effectiveness of procedures for controlling dust mites.

In 2009-2010, Associate Prof. Anchalee Tuntongchitra and Assistant Prof. Nat Malainual took over the leadership of SDMC and publicized it as a Dust Mite Biological Resource Center in collaboration with the Arthropods of Medical Importance Resource Bank, Institute of Tropical Medicine, Yonsei University, College of Medicine, Korea.

From the past until the present, Mahidol University has been the leader of "all things dust mite" and the **Siriraj Dust Mite Center** has been acknowledged as the premier Center for studying house dust mites in Southeast Asia. Our efforts focus on controlling house dust mites, on testing, analyzing and culturing dust mites on a large scale and the training of business or medical/scientific personnel.

ACKNOWLEDGEMENTS

We thank our Mite team; Mr. Teerapong Wangapai, Ms. Prapakorn Ninsanit, Ms. Hatai Nochote, Mr. Kajohnsak Norasri and Ms. Cholthicha Pongpleum for their technical assistance and efforts.

REFERENCES

1. Wongsathayuthong S, Lakshana P. House-dust mite survey in Bangkok and other provinces in Thailand. *J Med Assoc Thai*. 1972 May;55(5):272-86.
2. Malainual N, Vichyanond P, Phan-Urai P. House dust mite fauna in Thailand. *Clin Exp Allergy*. 1995 Jun;25(6):554-60.
3. Wongsathayuthong S. House mites and allergic bronchial asthma. *J Med Assoc Thai*. 1971;54:411-13.
4. Tuchinda M, Habanananda S, Vareenil J, Srimaruta N, Piromrat K. Asthma in Thai children: a study of 2000 cases. *Ann Allergy*. 1987 Sep;59(3):207-11.
5. Tungtrongchitr A, Sookrung N, Munkong N, Mahakittikun V, Chinabut P, Chaicumpa W, et al. The levels of cockroach allergen in relation to cockroach species and allergic diseases in Thai patients. *Asian Pac J Allergy Immunol*. 2004 Jun-Sep;22(2-3):115-21.
6. Sookrung N, Diraphat P, Chaicumpa W, Tongtawe P, Sakolvaree Y, Tapchaisri P, et al. Cockroach allergen detection and cockroach allergens of allergic Thai allergic patients. *Asian Pac J Allergy Immunol*. 2003 Mar;21(1):1-9.
7. Pumhirun P, Towiwat P, Mahakit P. Aeroallergen sensitivity of Thai patients with allergic rhinitis. *Asian Pac J Allergy Immunol*. 1997 Dec;15(4):183-5.
8. Mahakittikun V, Pattanachitvilat S, Nochot H, Bunnag C. Innovative method for rapid isolation of live dust mites with high purity. *J World Allergy Organization*. 2003;S1:157.
9. Mahakittikun V, Bunnag C, Vichyanond P, Komoltri C, Wongkamchai S, Tunsuriyawong P, Jareoncharsri P, Wimolwattanapun S, Manochun C. A Comparative study of the major allergenic components in house dust mite extracts between Siriraj and commercially prepared extracts. *Siriraj Gaz Hosp*. 2003;55:283-93.
10. Mahakittikun V, Wongkamchai S, Ahamad MH, Vichyanond P. Killing mites with heat. *Allergy*. 2001 Mar;56(3):262.
11. Mahakittikun V, Tze Ming H, Nochot H. Cloth can protect against house dust mite. *Siriraj Hosp Gaz*. 2001;53:27-33.
12. McLaughlin T, Vaughan JW, Perzanowski M, Platts-Mills TAE. Effect of fabric pore size in blocking cat and dust mite allergen. *J Allergy Clin Immunol*. 1998;101(Suppl): S167.
13. Frederick JM, Warner JO, Jessop WJ, Enander I, Warner JA. Effect of a bed covering system in children with asthma and house dust mite hypersensitivity. *Eur Respir J*. 1997 Feb;10(2):361-6.
14. Mahakittikun V, Komoltri C, Nochot H, Angus AC, Chew FT. Laboratory assessment of the efficiency of encasing materials against house dust mite and their allergens. *Allergy*. 2003 Oct;58(10):981-5.
15. Mahakittikun V, Komoltri C, Nochot H, Insung A, Wongkamchai S, Soonthornchareonnon N, Vichyanond P. Comparison of different apparatus for the assessment of anti-mite agents. *J Trop Med Parasitol* 2003;26:93-7.
16. Mahakittikun V, Jirapongsananuruk O, Nochot H, Boitano JJ, Tungtrongchitr A. Woven material for bed encasement prevent mite penetration. *J Allergy Clin Immunol*. 2003 Dec;112(6):1239-41.
17. 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 Nov;118(5):1164-8.
18. Wongkamchai S, Uppanisakorn M, Mahakittikun V, Nochote H, Chinabuthra P. Laboratory study of effectiveness of pyrethrin and benzyl benzoate as acaricides for control of house dust mites. *Chiang Mai Med Bull*. 2002;41(1):43-50.
19. Wongkamchai S, Rongsriyam K, Nochot H, Mahakittikun V, Sermart B, Choochote W, et al. Efficacy of various synthetic pyrethroid-impregnated encasement materials against house dust mite under laboratory conditions. *Exp Appl Acarol*. 2005;35(4):293-300.
20. Chirdjirapong V, Pootong V, Ruangrak S, Mahakittikun V, Kolmontri C, Visitsunthorn N, Vichyanond P. House dust mite allergens accumulate more rapidly in synthetic and kapok mattresses than in coconut and sponge mattresses. Presented in the American Academy of Allergy Asthma & Immunology Conference, New York, USA, 2002.
21. Soonthornchareonnon N, Mahakittikun V, Chuakul Wongsatit, Rongsriyam K. Acaricide activity of Thailand medicinal plants. *Thai Phytopharm*. 2005;12:1-7.
22. Soonthornchareonnon N, Sakayarojkul M, Isaka M, Mahakittikun V, Chuakul W, Wongsinkongman P. Acaricidal Daphnane Diterpenoids from *Trigonostemon reidioides* (KURZ) CRAIB roots. *Chem. Pharm. Bull*. 2005;53(2):241-3.