

Pioneers and Milestones

The history of the finding of the house dust mite

The identification of mites of the genus *Dermatophagoides*, now mostly referred to as house dust mites, was the result of the combined thinking and working of medical doctors during a pre-World War II period and a revival of this work by a team of brilliant scientific minds supported by solid allergologic and biologic expertise. The first fully documented publication on the significance of house dust mites for allergic respiratory diseases worldwide was published in this Journal in 1967.¹ The historical facts and events leading to this finding are summarized in this professional-biographic sketch of some of the persons involved.

Storage mites, "bed mites," 1924-1961. When Reindert Voorhorst started his clinical and research work on respiratory allergy at the ear, nose, and throat department of the "Academic Hospital Leiden" (now Leiden University Medical Center) in 1956, he saw that until some time in the 1940s, an extract of "bed mites"² had been included in the standard panel of diagnostic skin tests. Symptoms of respiratory allergy caused by mites had been the subject of scientific interest in the years 1924 through 1930, when the Leiden pharmacologist Willem Storm van Leeuwen described a number of cases of mite-related allergic asthma (eg, in farmers after having been exposed to mite-infested wheat or oat).³ Storm van Leeuwen and his coworkers speculated that mites could also be involved in the origin of the mysterious "house dust allergen," which was particularly present in dust from damp houses, suggesting a biologic process. However, they were unsuccessful in proving the relationship between mites and the allergenic properties of house dust. After the death of Storm van Leeuwen, research on mite-related respiratory allergies was discontinued, and in the years 1940 through 1945 of the Second World War, almost all scientific work in The Netherlands was seriously hampered.

Voorhorst, who was a specialist in internal medicine, became very much interested in the origin of the house dust allergen to which so many of his patients appeared to be allergic. Together with a former assistant of Storm van Leeuwen, Hendrik Varekamp, Voorhorst began to study several possible biologic sources of this allergen, such as fungi, animal skin scales ("dander"), insects, and also mites. The taxonomic identity of the "bed mites" was, and still is, unknown, and therefore he consulted acarologists (mite specialists) with the question of what mites were most likely to live in house dust. In September 1959, Voorhorst visited the Pest Infestation Laboratory in Slough (near London, United Kingdom), a laboratory that specialized in storage

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Prof Dr Reindert Voorhorst (1915)

Initially trained in internal medicine and microbiology, Reindert Voorhorst became attached as an allergologist to the University Hospital, Leiden, The Netherlands (today known as Leiden University Medical Centre), in 1956. His main interest was directed toward what he called the atopic syndrome. Voorhorst believed there were 2 prerequisites for his investigations: (1) the introduction of the quantitative factor in intracutaneous skin testing by means of the application of 10-fold extract dilutions and (2) a method to express the allergen content of extracts as "equivalent units."⁴ Skin testing with dilution series was applied in the comparison of house dust and house dust mite extracts.⁵ The conclusion of Voorhorst et al¹ that the *Dermatophagoides* species mite was the main allergenic source in house dust had a global significance. First, the problem of the house dust allergen seemed to be solved. Second, this mite species could be identified in house dust samples from all over the world. At the European Congress of Allergology and Clinical Immunology in Berlin (1968), the presentation on the house dust mite by Voorhorst caused a commotion. Other investigations, in the end, have confirmed his findings.



insects and mites. There he obtained samples of 3 common stored-food species of mites, which were considered to be most widespread also in homes.

In the meantime, Voorhorst had acquired a broad knowledge of the nature of allergic diseases, which he put together in 1962 in a book, *Basic Facts of Allergy*.⁶ In the last chapter he summarized the results of his skin test studies with extracts of the 3 storage mites *Tyrophagus castellani* (now

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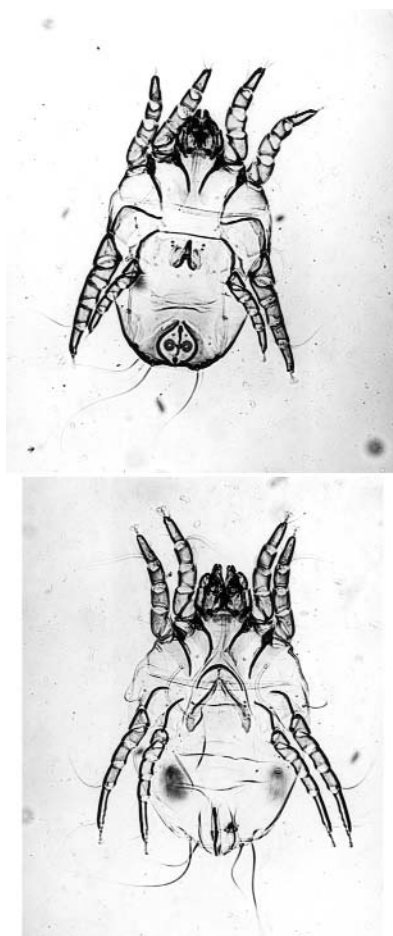


FIG 1. *Dermatophagoides pteronyssinus*: top, male; bottom, female (body length = $\pm 320 \mu\text{m}$).

Tyrophagus putrescentiae), *Glycyphagus domesticus*, and *Tyroglyphus farinae* (now *Acarus siro*). The results gave him the conviction that these mite species, although they were sources of potent allergens, were not the origin of the house dust allergen. Still, he believed in a biologic source and was rather skeptical about alternative hypotheses on the biochemical degradation in dust leading to its allergenicity, as postulated by the chemist Luc Berrens⁷ of the Dermatology Department of the Utrecht University Hospital. Voorhorst decided to look further for other mites, particularly in house dust itself, rather than to go on with storage mites.

Involvement of biologists. Beginning in 1962, Voorhorst sought the help of the zoologic ecologist Prof Don Kuenen, who suggested that a student working for her MSc degree would simply and directly look for mites in house dust, applying documented extracting methods used in agroentomologic studies. This student, Marise Boezeman, very soon found small mites, which on inspection under the microscope and after consultation with the acarologist of the national

Prof Dr Willem Storm van Leeuwen (1883–1933)

Willem Storm van Leeuwen was professor of pharmacology and director of the Pharmacotherapeutic Institute at the University of Leiden, The Netherlands, from 1920. At that time, he became mainly interested in allergy and asthma and started investigations in this field. He and his coworkers realized that “climate allergens” determined by dampness and temperature could play a crucial role in asthma symptomatology.^{8,9}



They concluded that the conditions of the floors and walls of houses, as well as the superficial layers of the earth, were important in this respect. It was also clear that many asthmatic patients improved spontaneously when hospitalized in a clean room with regularly sterilized mattresses.⁹ Later, he established his Clinic of Allergic Diseases in 2 rented houses in Leiden. Here he could realize allergen-free rooms by using much technical equipment.^{8,10} He also designed similar rooms for patients' houses. A compilation of the investigations by Storm van Leeuwen and coworkers in relation to house dust can be found in the article in the *Journal of Allergy* by Voorhorst et al.¹ House dust and certain other dust extracts as from old kapok produce skin reactions in many persons all over the world. Complaints by patients are more prominent from July to November, which corresponds with the increased allergenic concentration of house dust extracts in the same period. Poorly constructed houses and houses on peat and clay with a high water level are bad for asthmatic patients, whereas houses on sandy soil and in high mountains are much better.

Storm van Leeuwen's basic assumption that allergy and asthma were interrelated in many patients encountered much resistance in the Netherlands. This energetic, critical, and sincere person died too early at the age of 50.

Natural History Museum, appeared to be not one of the earlier mentioned species but rather an unknown one. She also found that there were clearly more mites in the dust from a damp house parallel with the allergen content. Voorhorst was very much determined to prove that this was indeed the mite he had been seeking for so many years. After having presented this rather unknown mite to several acarologists in The Netherlands and abroad, it was provisionally classified to genus level as *Dermatophagoides* species.

Dr Hendrik Varekamp (1896-1971)

After receiving his medical degree, Hendrik Varekamp was trained at the institute of the pharmacologist Prof Dr W. Storm van Leeuwen at the University of Leiden, The Netherlands, in 1920. He later became a coworker until 1932. His scientific work in this institute was directed at house dust as a "climate allergen." His investigations were recorded together in his thesis, "The exogen causes of asthma."¹¹ From 1932 to 1956, he practiced general medicine near Leiden and continued his investigations on the dampness of houses of patients with rheumatic disorders and asthma. From 1956, he was attached to the Department of Allergology of the Leiden University Hospital for asthma epidemiology and for the search for the main factors that determine the allergenicity of house dust.¹² His investigations on the role of the construction of houses were performed with the help of the construction engineer Maarten J. Leupen and the technician Ankie W. Lyklema. Their results constituted an essential contribution to the article of Voorhorst et al¹ in the *Journal of Allergy* about the house dust mite.



Marise Boezeman finished her biologic education and obtained her MSc degree in 1963, after which she did preparative work on the laboratory cultivation of these mites to produce source material for allergenic extracts. Then she decided to make a career as a teacher in general biology. Voorhorst energetically continued his allergologic work, and at the end of 1963, he invited Frits Spieksma, also with an MSc in biology, to expand the ecologic studies of this intriguing mite and to start mass culturing for the production of source material.

The collaboration between the allergologist Voorhorst and the ecologist Spieksma was rather successful and resulted in many original findings and conclusions, showing that this then-unknown mite was indeed the "producer of the house dust allergen."

Publications and international acceptance. Voorhorst could not wait to report the first results until all the pieces of the puzzle were in place, and at a European Allergy Congress in Spain, he found the editor of the rather obscure East German allergy journal *Allergie und Asthma* willing to publish the first findings on this controversial topic as a preliminary report in 1964.¹³ Voorhorst was very self-confident about his

Marise Spieksma-Boezeman (1938-)

Marise Spieksma-Boezeman studied zoology and botany at the University of Leiden, The Netherlands. Her final MSc project resulted in 1962 in the original identification of a mite of the genus *Dermatophagoides* in samples of house dust, a hardly known organism.¹³ Moreover, a quantitative relationship between the skin reactivity with extracts of these dust samples and the number of mites could be established.¹ She also developed laboratory cultures of these mites. Long before, Dekker¹⁴ found several kinds of mites in the house dust of asthmatic patients, although he could identify only a part of them. After her study, Ms Spieksma trained students in her discipline at the university. Later, she became a teacher at a regional secondary school until her retirement. Her investigations on mites were continued by her husband Frits ThM Spieksma, the aerobiologist at the Department of Allergology, University Hospital, Leiden, Netherlands.



finding of the source of the house dust allergen, and sometimes he had difficulty accepting that some colleagues were rather skeptical in adopting his new revolutionary conviction. At several national (Dutch) and international scientific meetings, there were excited discussions between believers and nonbelievers of the mite origin of the house dust allergen. The mite was classified to species level as *Dermatophagoides pteronyssinus* (Fig 1) by the Belgian acarologist Alex Fain.¹⁵

The first fully documented manuscript was submitted to the *Journal of Allergy* in July 1966 and published in June 1967,¹ the same month that Frits Spieksma took his PhD at the University of Leiden. Other coauthors of this publication were Hendrik Varekamp, who bridged to Storm van Leeuwen's knowledge of the 1920s and did most of the epidemiologic work; Maarten Leupen, the house building engineer responsible for the dampness classification of the houses concerned; and Ms Ankie Lyklema, technician, who did part of the dust sampling and processing in the laboratory.

The first appreciation of the new idea of mites as the origin of the house dust allergen came from Jack Pepys, and other groups quite soon published confirmative reports.¹⁶⁻¹⁹

Simultaneously with the Dutch preliminary report in December 1964,¹³ a Japanese biologist, Shiro

Frits Th.M. Spieksma (1936-)

Frits Spieksma studied zoology and botany at the University of Leiden, The Netherlands. From 1963, he worked at the Department of Allergology, led by Professor Dr R. Voorhorst, University Hospital, Leiden. After the closure of the Department of Allergology in 1982, he continued his work at the Department of Pulmonology, from 1986 as associate professor of allergologic aerobiology. He was head of the Laboratory of Aerobiology from 1980 until his official retirement in 1999. He remained active as an honorary staff member until 2003. From 1963 until 1973, Frits Spieksma was mainly involved in the ecology and biology of the allergen producing house dust mite of the *Dermatophagoides* genus¹ as a continuation of the first identification of that mite by his wife, Marise Spieksma-Boezeman.¹³ Afterwards, this field continued to hold his interest.²⁰⁻²² In 1973, he started investigations on air-borne pollen in relation to pollinosis as another successful field.²³⁻²⁵



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Oshima, looking for parasites causing skin afflictions in schoolchildren in Yokohama, reported the finding of *Dermatophagoides* species in "tatami" floor coverings.²⁶ Contacts with the Japanese colleagues resulted in the first confirming report from outside Europe.²⁷

Since then, the number of publications on house dust mite allergy has been growing almost exponentially. The fact that the allergenic properties of house dust originate from its content of populations of house dust mites, mostly of the genus *Dermatophagoides*, has become common knowledge, even outside the medical profession. However, very few recent reports refer to the original publication of 1967.¹

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