

Regulatory Action Criteria for Filth and Other Extraneous Materials

II. Allergenic Mites: An Emerging Food Safety Issue

Alan R. Olsen¹

Microanalytical Branch, HFS-315, Center for Food Safety and Applied Nutrition, U.S. Food and Drug Administration,
200 C Street, Southwest, Washington, DC 20204

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Four species of food-contaminating mites have recently been reported to have caused IgE-mediated allergic reactions, including anaphylaxis, in persons who consumed mite-contaminated foods. The mite species are the American house dust mite, *Dermatophagoides farinae* Hughes (Acarina: Pyroglyphidae); the scaly grain mite, *Suidasia* sp. prob. *pontifica* Oudemans (Acarina: Suidasiidae), an acarid mite, *Thyreophagus entomophagus* Portus & Gomez (Acarina: Acaridae); and the mold mite, *Tyrophagus putrescentiae* (Schränk) (Acarina: Acaridae). Allergenic mites are an emerging food safety issue as ingested allergens in mite-contaminated food.

INTRODUCTION

More than three decades ago, scientists reported the discovery that allergens from the European house-dust mite, *Dermatophagoides pteronyssinus* (Trouessart), and the American house-dust mite, *Dermatophagoides farinae* Hughes (Acarina: Pyroglyphidae), were causative agents of asthma and other allergy diseases in people who are sensitized to house dust (Voorhorst *et al.*, 1964; Maunsell *et al.*, 1968; Spieksma and Spieksma-Bozeman, 1967; Larson *et al.*, 1969; Mitchell *et al.*, 1969). In 1978, reactions to allergens from these mites were shown to be IgE-mediated (Chapman and Platts-Mills, 1978). Soon, the stored product mites *Tyrophagus putrescentiae* (Schränk) (Acarina: Acaridae) and *Lepidoglyphus destructor* (Schränk) (Acarina: Glycyphagidae) were also demonstrated to be allergenic (Green and Woolcock, 1978; Wraith *et al.*, 1979).

At first, the association of mites with allergies met with skepticism; however, a large body of clinical and research literature has firmly established that these mites are allergenic and that they play a significant role in the causation of house-dust asthma and other

house-dust allergy diseases (Mulla and Medina, 1980). The connection between asthma and mites is so firmly established that commercially prepared extracts of mite allergens are available for use in the diagnosis and treatment of house-dust asthma and other house-dust allergy diseases (Wharton, 1970). These extracts are used by physicians throughout the world on a regular basis to diagnose and treat mite allergies (Arlian, 1991). Wirtz (1984) and Wharton (1976) conservatively estimated that 4% of the U.S. population is sensitized to house-dust mite allergens.

Until very recently, it was not suspected that ingestion of these mites could cause serious illness, despite their potent inhalant and contact allergenicity. Recently, however, a number of reports have been published that establish allergenic mites as the causative agents of allergy-induced anaphylaxis in persons who consumed mite-infested food. The new reports identify allergenic food-infesting mites as an emerging food safety issue of concern to health care providers as well as government agencies that regulate food safety (Pugh, 1996).

METHODOLOGY

Reviews of the literature covering the period prior to 1990 (Ishi, 1975; Lang *et al.*, 1976; Wharton, 1976; Arlian *et al.*, 1979; Mulla and Medina, 1980; Wirtz, 1984; Guerin, 1990; Arlian, 1991) contain no references to mites as ingestant allergens. For this study, literature searches were conducted for the period 1990 to present using Medline and Biosis databases. In addition, the U.S. Food and Drug Administration (FDA) Health Hazard Evaluation Board was contacted for records of Board decisions involving mites in food. The recent literature concerning mites as ingested allergens is discussed below, with background material supplied from the earlier review articles and other publications. This report is the second of a series in the development of a transparent science base for a revised

¹ Assisted by Sherry A. Knight.

FDA regulatory policy in the area of filth and extraneous materials in food.

SUMMARY OF LITERATURE REPORTS

Intestinal Acariasis

Over the years, a scattering of incidents of diarrheal disease have been reported to be associated with mite-infested food (e.g., Hinman and Kampmeier, 1934). The authors of the reports based their conclusions that mites caused diarrhea or other symptoms on observations of mites in stool samples and on observations that the symptoms ceased after the mites were purged from a patient's gastrointestinal tract. The symptoms of intestinal acariasis (diarrhea, gastroenteritis) were not attributable to an allergic reaction to the mites until Scala (1995) found that ingested mite allergens alone may induce gastroenteritis in sensitized individuals. It is still uncertain whether diarrheal disease attributed to acariasis is an allergy-related syndrome.

Oral Allergy

Liccardi *et al.* (1996) reported a case of oral allergy syndrome (oral pruritus, swelling of lips, tongue, and throat) associated with consumption of salami. The patient was monosensitive to allergens from *D. farinae* and *D. pteronyssinus*. The authors of this report originally concluded that allergy to a dried pork ingredient in the salami was the cause of illness; however, others (Armentia and Vega, 1997) hypothesized that mites were a more likely cause based on the originally reported results of skin prick and oral challenge tests. The original authors agreed that the evidence was equivocal because the salami product was not examined for mite infestation (Liccardi and D'Amato, 1997). Oral sensitization to mite allergens has been observed in clinical settings during allergy therapy treatments (Matsumoto *et al.*, 1996a; Wortman, 1977).

Anaphylaxis

Of greatest concern, however, are the recent reports of persons suffering moderate to severe systemic reactions, or anaphylaxis, as a result of consuming food that was infested with allergenic mites. These reports are compelling in that specific mites are established by rigorous clinical tests to be the cause of allergen-induced anaphylaxis.

Erban *et al.* (1993) reported a case of anaphylaxis in a man who had eaten baked goods infested with live *D. farinae* mites. Skin prick tests eliminated all food ingredients as the cause of the illness. The man was found to be highly sensitive to *D. farinae* and *D. pteronyssinus* allergens by enzyme-linked immunosorbent assay (ELISA) testing, confirmed by radioallergosorbent test (RAST) results.

Matsumoto *et al.* (1996b) reported two cases of anaphylaxis in children (11 and 14 years old) from eating mite-infested food. In one of the cases the anaphylaxis was classified by the attending physicians as life-threatening. Both cases involved baked products made from infested flour. Skin prick tests on both patients ruled out all ingredients of the suspect foods as the cause. These results were confirmed by total serum immunoglobulin E (IgE) and RAST testing. Oral provocation tests with identical but uninfested food found no allergic reaction. The patients were found to be sensitive to mite allergens by serum-specific IgE titration. Both were sensitive to allergen extracts from the mites *D. pteronyssinus*, *D. farinae*, and *T. putrescentiae*. One patient was also sensitive to *Acarus siro* L. (Acarina: Acaridae) allergen. In both cases, the flour ingredient of the food was infested with *T. putrescentiae* at levels of 110 and 140 mites per 10 mg of product.

Blanco *et al.* (1997a) conducted a study of patients who suffered anaphylaxis after ingestion of food containing mite-infested flour. Skin prick and total serum IgE tests were used to screen subjects. Sixteen patients who had experienced anaphylaxis had no sensitivity to flour allergens but high sensitivity to mite allergens, with six confirmed by oral food challenge tests (only six were challenge tested). All six showed a history of respiratory allergy to house-dust mites. Three of the oral challenge tests resulted in systemic reactions to mite-infested food while none of the control flour challenges yielded allergy reactions. Samples of flour from foods consumed by four of the six patients were found to be infested with *D. farinae* (one sample) or *Thyreophagus entomophagus* (Laboulbene) (Acarina: Acaridae) (three samples). The food infested with *D. farinae* was found to contain allergens of the mite as well as the mites themselves. The authors concluded that ingestion of food contaminated with mites may induce systemic anaphylactic reactions in patients with respiratory allergy to mites. The same research group issued a contemporaneous report that demonstrated the inducement of asthma by ingestion of food made with mite-contaminated flour (Blanco *et al.*, 1997b).

Sanchez-Borges *et al.* (1997) conducted a similar study using skin prick tests to screen patients. Of 30 patients who suffered "acute" IgE-mediated anaphylaxis from food made with mite-contaminated flour, all gave negative skin prick test responses for uncontaminated flour and other food extracts but positive responses for infested flour. Flour or bread samples from these patients contained the mites *D. farinae* (28 samples of flour) or *Suidasia* sp. prob. *pontifica* Oudemans (Acarina: Acaridae *sensu lato*) (2 samples of bread) and their allergens. The study demonstrated the heat stability of mite allergens by repeating skin prick tests with mite-contaminated flour that had been heated to 100°C. The tests indicated positive reactions from the

TABLE 1
Examples of Common Allergenic Mites

Mite species	Literature references
<i>Acarus siro</i> L.	Wraith <i>et al.</i> , 1979 Luczynska <i>et al.</i> , 1990
<i>Aleuroglyphus ovatus</i> (Troupeau)	Puerta <i>et al.</i> , 1993
<i>Blomia kulagini</i> Zachvatkin	Armentia <i>et al.</i> , 1997
<i>Blomia tropicalis</i> van Bronswijk, de Cock and Oshima	Arlian <i>et al.</i> , 1993
<i>Chortoglyphus arcuatus</i> (Troupeau)	Puerta <i>et al.</i> , 1993
<i>Dermatophagoides farinae</i> Hughes	Wharton, 1976 Armentia <i>et al.</i> , 1997
<i>Dermatophagoides pteronyssinus</i> (Trouessart)	Wharton, 1976
<i>Euroglyphus maynei</i> (Cooreman)	Colloff, 1991
<i>Gohieria fusca</i> (Oudemans)	Boner <i>et al.</i> , 1989
<i>Glycyphagus domesticus</i> (DeGeer)	Woodcock and Cunningham, 1980 Wraith <i>et al.</i> , 1979
<i>Lepidoglyphus destructor</i> (Schrank)	Wraith <i>et al.</i> , 1979 Pollo Corrales, 1997
<i>Suidasia pontifica</i> Oudemans	Sanchez-Borges <i>et al.</i> (1997)
<i>Thyreophagus entomophagus</i> (Laboulbene)	Blanco <i>et al.</i> (1997a)
<i>Tyrophagus longior</i> (Gervais)	Luczynska <i>et al.</i> , 1990
<i>Tyrophagus putrescentiae</i> (Schrank)	Arlian <i>et al.</i> , 1984a Green and Woolcock, 1978

heated flour. The authors concluded that systemic anaphylaxis can occur after ingestion of heated or unheated mite-contaminated food.

In three of the above clinical studies (Matsumoto, Blanco and Sanchez-Borges), the researchers used established, standardized medical tests and procedures (*cf.* Sampson, 1996) to diagnose the IgE-mediated mechanisms involved in the allergic reactions that they reported.

**MEDICAL IMPORTANCE OF ALLERGENIC MITES:
EVIDENCE FOR IgE-MEDIATION**

Certain mites possess powerful aeroallergens in their bodies as well as in their secretions and excrement (Wharton, 1976; Woolley, 1988; Evans, 1992). These allergens are the cause of a considerable amount of allergic rhinitis, asthma, and eczema (Godard, 1993; Mulla and Medina, 1980; Wharton, 1976). Reactions to the aeroallergens from these mites have been convincingly demonstrated to be IgE-mediated allergic reactions (Wharton, 1976; Chapman and Platts-Mills, 1978; Green and Woolcock, 1978; Arlian *et al.*, 1993; Boner *et al.*, 1989; Luczynska *et al.*, 1990; Colloff, 1991; Arlian *et al.*, 1993; Puerta *et al.*, 1993; Armentia *et al.*, 1997; Pollo Corrales, 1997). Table 1 lists examples of mites that cause IgE-mediated allergic reactions.

Prior to the publication of the report from Erban *et al.* (1993), there were no published studies involving possible reactions to allergenic mites in food that de-

finitively ruled out allergies to food ingredients as factors in the matrix of allergic reactions to things that are eaten. The Erban report demonstrated that systemic allergic reactions can be caused solely by ingestion of these mites. Matsumoto *et al.* (1996b), Blanco *et al.* (1997a), and Sanchez-Borges *et al.* (1997) confirmed this observation and demonstrated that the reactions to ingested mites are true IgE-mediated allergic reactions. Ingested mite allergens may also be sufficiently heat-stable that they are not removed or denatured by cooking (Sanchez-Borges *et al.*, 1997). The Matsumoto, Blanco, and Sanchez-Borges reports scientifically document mite-induced, IgE-mediated, systemic allergic reactions in a combined total of 36 different patients for whom food ingredients and other allergenic factors were ruled out. These recent clinical reports are a compelling indication that mites as ingestant allergens are a significant emerging issue in allergy disease.

By contrast, a total of four cases of mite-contaminated food have been submitted to the FDA Health Hazard Evaluation Board for consideration over the past decade. No illnesses or injuries were associated with these cases. In each case, the Board determined that no hazard existed, but the Board decisions predate the availability of the clinical case histories that document IgE-mediated allergic reactions to ingested mite contaminants. Although no deaths from mite-contaminated food have been reported in the literature or to FDA, attending physicians for the literature reports cited above classified their patients' reactions to ingested mite allergens as moderate, serious, or life-threatening.

The discovery that an arthropod, such as a mite, that is known primarily as a producer of inhalant allergens can also produce allergens that induce systemic IgE-mediated reactions through ingestion is not without parallel. The cochineal insect, *Dactylopius coccus* Costa (Homoptera: Dactylopidae), is the source of a natural red dye that is used as a food coloring additive. Cochineal allergens may induce inhalant and contact allergic reactions including asthma and dermatitis (Quirce *et al.*, 1994; Guy *et al.*, 1995). Ingestion of food that contains the color additive (carmine) derived from cochineal insects may result in IgE-mediated anaphylaxis from the carmine additive (Kagi *et al.*, 1994; Beaudouin *et al.*, 1995; Baldwin *et al.*, 1997).

Other arthropods, notably cockroaches (Dictyoptera: Blattidae and Blattellidae), have recently been demonstrated to produce aeroallergens that are associated with increased morbidity from asthma (Rosenstreich *et al.*, 1997). In light of the discovery that ingested mite allergens cause allergic reactions in mite-sensitive asthmatics (Matsumoto *et al.*, 1996b; Blanco *et al.*, 1997a, b), it is reasonable to suspect that cockroach aeroallergens may be similarly involved in ingestive allergic reactions.

ALLERGENIC MITE SPECIES THAT CONTAMINATE FOOD

Food products are subject to infestation from a variety of mite pests. Hughes (1976) lists 64 species of mites as inhabiting stored food products. Smiley (1983) lists 114 species of stored product mites that infest food products. Pugh (1996) reported that 12 species of mites were isolated from 567 samples of cereal-based products sampled in the United Kingdom. Olsen (1983) found 22 species of mites as actual contaminants in 149 samples of processed foods analyzed by the FDA over a 2-year period. Table 2 lists the mites found during the FDA survey, in descending order of frequency of occurrence.

Eight of the above species (denoted by an asterisk) are known to induce IgE-mediated reactions in people as inhalant or contact allergens (Tee, 1994). Other common food-contaminating species (Hughes, 1976) that are known to possess similar allergenic properties include the dust mites *L. destructor* (Wraith *et al.*, 1979; van Hage-Hamsten and Johansson, 1992) and *Gohieria fusca* Oudemans (Boner *et al.*, 1989) (Glycyphagidae) and a cheese mite, *Tyrophagus longior* (Gervais) (Acaridae) (Luczynska *et al.*, 1990).

As documented in the case histories described previously, four of these food-contaminating mite species have been demonstrated to cause IgE-mediated anaphylaxis when ingested in contaminated food. Table 3 lists these mite species along with the literature references that document their ingestant allergenicity.

TAXONOMIES AND IDENTIFICATION

From a public health standpoint and from the perspective of the manufacture of diagnostic or therapeutic extracts, it is critical that the mites involved in cases of allergic reactions be identified precisely and accurately. Inaccurate mite identifications have resulted in FDA-monitored recalls of pharmaceutical extracts of mite allergens.

The four mite species listed in Table 3 belong to two taxonomic families, the Pyroglyphidae (*Dermatophagoides*) and the Acaridae (*Suidasia*, *Thyreophagus*, and *Tyrophagus*). Some acarologists place *Suidasia* spp. in the separate family Suidasiidae. The other allergenic species listed in Tables 1 and 2 belong to the families Pyroglyphidae (*Euroglyphus*), Acaridae (*Acarus*, and *Aleuroglyphus*), or Glycyphagidae (*Gohieria*, *Glycyphagus*, and *Lepidoglyphus*). All of these families belong to the suborder Astigmata, which are minute ($< \frac{1}{2}$ mm) arthropods requiring special skills and instruments for their accurate identification.

In all the case studies discussed previously, the attending physicians and clinicians submitted mite specimens to expert acarologists for identification. All of the mites listed in Tables 1 and 2 can be readily iden-

tified to the genus or species levels using standard identification manuals that include stored product mites (*i.e.*, Krantz, 1972; Hughes, 1976; McDaniel, 1979; Smiley, 1991; Olsen and Potter, 1996). Mulla and Medina (1980) published a bilingual, illustrated identification key for allergenic mites in Spanish and English. The identification of these mites requires a compound microscope capable of 400 $\times$ magnification with transmitted light. Phase-contrast microscopy to 400 $\times$ assists in examining some of the smaller micromorphological characters used to differentiate species. New species and new records of stored product mites are reported from time to time (Olsen, 1982a; Olsen, 1988; Potter and Olsen, 1987), requiring the identifier of allergenic mites to maintain awareness of current taxonomic literature in the field.

ALLERGENICITY THRESHOLDS FOR FOOD-CONTAMINATING MITES

Studies involving mite aeroallergens suggest that exposure to a level as low as 2 μ g of mite allergen per gram of house dust is a risk factor for the development of asthma (Sporick and Platts-Mills, 1992; Tovey, 1992; Platts-Mills and Carter, 1997; Rosenstreich *et al.*, 1997). This corresponds to approximately 100 mites per gram of dust (Sporick and Platts-Mills, 1992). Levels over 10 μ g of mite allergen per gram of dust (approximately 500 mites per gram) reportedly "exacerbate" asthma symptoms (Platts-Mills and De Weck, 1989; Sporick and Platts-Mills, 1992). Bronchial responses have been observed in asthmatics who inhaled as little as 20 ng of mite allergens in 6 min (Tovey *et al.*, 1981). Wharton (1976) suggests a "sanitary standard" of 12 mites per 0.5 m² for textiles and bedding used by mite-sensitive asthmatics and for seats in public carriers.

Little is known about the levels of mites that are necessary to trigger an allergic reaction upon ingestion. Matsumoto *et al.* (1996b) reported extremely high levels of *T. putrescentiae* ranging from 110 to 140 mites per 10 mg of the infested products which induced anaphylaxis when eaten. The analytical method used to derive these numbers was an adaptation of one of the techniques used to extract mites from dust samples. These techniques are reviewed by Bischoff *et al.* (1992). The techniques are designed for two-dimensional sampling from surfaces of textiles, walls, and floors. Because the allergens are primarily contained in mite feces (Arlian, 1991; Evans, 1992), numbers of mites may not always correlate to allergen levels in an infested food. Duration of infestation may disproportionately increase the ratio of allergens from the mite feces in infested products (Mitchell *et al.*, 1969). The Matsumoto numbers were derived from product that was submitted to the researchers days after the incidents of anaphylaxis occurred, providing the live mite popula-

TABLE 2
Examples of Mites Found by FDA in Processed Food Samples (from Olsen, 1983)

Species	Common name	No. samples
<i>Tyrophagus putrescentiae</i> (Schrank) ^a	Mold mite	43
<i>Lardoglyphus kono</i> (Sasa & Asanuma)	Dried fish mite	37
<i>Suidasia pontifica</i> Oudemans ^a	Scaly grain mite	26
<i>Carpoglyphus lactis</i> (L.)	Dried fruit mite	18
<i>Aleuroglyphus ovatus</i> (Troupeau)	Brown-legged grain mite	14
<i>Caloglyphus</i> spp. (two species)	—	11
<i>Dermatophagoides pteronyssinus</i> (Trouessart) ^a	European house-dust mite	10
<i>Thyreophagus gallegoi</i> Portus & Gomez	—	8
<i>Acarus siro</i> L. ^a	Grain mite	7
<i>Euroglyphus maynei</i> (Cooreman) ^a	Mayne's house-dust mite	5
<i>Histiogaster</i> sp.	—	5
<i>Chortoglyphus arcuatus</i> (Troupeau)	—	4
<i>Lepidoglyphus fustifer</i> (Oudemans)	—	4
<i>Lardoglyphus angelinae</i> Olsen	Angelina's dried fish mite	3
<i>Suidasia nesbitti</i> Hughes	Nesbitt's scaly grain mite	2
<i>Thyreophagus entomophagus</i> (Laboulbene) ^a	Museum mite	2
<i>Klemania plumosus</i> (Oudemans)	—	2
<i>Glycyphagus domesticus</i> (DeGeer) ^a	House mite	1
<i>Lardoglyphus zacheri</i> Oudemans	Hide mite	1
<i>Dermatophagoides farinae</i> Hughes ^a	American house-dust mite	1
<i>Macrocheles muscaedomesticae</i> (Scopoli)	House fly mite	1

^a Known producer of allergens (Tee, 1994).

tions in the product an opportunity to increase, migrate within the product, or even disperse.

Using standard food analytical techniques (Boese and Cichowicz, 1995) for larger portion sizes that take into account the entire contents of a food container, the highest numbers of mites that FDA analyses have found are levels as high as 6000 to 40,000 mites per 3600 g (0.16–1.1 mites per 10 mg) of food sample (Olsen, 1982b). Products analyzed by FDA and found to be contaminated rarely reach the marketplace, so FDA analytical data cannot be correlated to morbidity statistics in the general population.

Mites tend to congregate on food product surfaces (Solomon, 1945), making it unlikely that numbers derived from small amounts of surface material represent a true picture of the ratio of mites to amount of food product that is necessary to trigger an allergic reaction. It is unknown whether the mites reported by Matsumoto were evenly distributed at levels of 110 to 140 mites per 10 mg throughout a typical 50-g serving portion of the products. By comparison, estimated levels of 5000 to 8000 mites per gram of house dust (50–80 mites per 10 mg) have been reported from carpets and bedding, ranging up to 11,000 mite per gram on rare occasions (Mumcuoglu, 1976; Wharton, 1976). Mite infestations of foodstuffs rarely approach 1% of product by volume (Solomon, 1945).

Even less is known about the actual levels of mite allergens necessary to trigger an allergic reaction via ingestion. Marcucci *et al.* (1985) report ambiguous results for correlation of levels of mite allergens from intestinal washings and serum titrations. Beaudouin

et al. (1995) found that ingestion of 1 mg of carmine, a concentrated extract of allergenic cochineal insects, triggers anaphylaxis in sensitized individuals. This level of precision (1 mg) is possible because the amounts of intentionally added food ingredients, such as carmine, are often precisely known. One milligram of allergenic mites is approximately 280–300 mites (Solomon, 1945). This figure resembles the 500 mites per gram of dust that was suggested by Sporick and Platts-Mills (1992) as an inhalant triggering exposure level in asthmatics.

CROSS-REACTIVITY

Cross-reactivity between allergens from different species of allergenic mites or between these and various food allergens has been reported in the literature (*e.g.*, Arlian *et al.*, 1984b; Carrillo *et al.*, 1994; Castillo *et al.*, 1996; De Maat-Bleeker *et al.*, 1995; Luczynska *et*

TABLE 3
Allergenic Mites Associated with Ingestive IgE-Mediated Anaphylaxis

Species	Literature references
<i>Dermatophagoides farinae</i>	Erban <i>et al.</i> , 1993; Blanco <i>et al.</i> , 1997a Sanchez-Borges <i>et al.</i> , 1997
<i>Suidasia</i> sp. prob. <i>pontifica</i>	Sanchez-Borges <i>et al.</i> , 1997
<i>Thyreophagus entomophagus</i>	Blanco <i>et al.</i> , 1997a
<i>Tyrophagus putrescentiae</i>	Matsumoto <i>et al.</i> , 1996b

al., 1990; van Ree *et al.*, 1996). In her review of the literature, Tee (1994) notes that there are also reports that demonstrate a lack of cross-reactivity between many of the same allergens. The body of data in the literature concerning cross-reactivity has proven ambiguous to date, but Tee points out that the allergens found in house-dust mites (family Pyroglyphidae) are chemically distinct from the allergens found in stored product mites (family Acaridae).

The question of cross-reactivity is further complicated by the existence of three distinct groups of mite allergens, each group with different etiologies and different stabilities (Arlian, 1991). Cross-reactivity among allergenic mites is thought to occur primarily between allergens that belong to the same group. Group I allergens occur in mite feces and are sensitive to heat and pH. The allergens have protein sequence homology with thiol proteases such as papain. Group II allergens are found in mite feces and mite bodies. They are both heat and pH resistant. Group II mite allergens have no homology with other known proteins. Relatively little is known about group III mite allergens except they have partial protein sequence homology with serine proteases such as trypsin and chymotrypsin (Sporick and Platts-Mills, 1992).

SEAFOOD

Seafood Hazard Analysis and Critical Control Point (HACCP) regulations create a special need for awareness of the potential hazards associated with any reasonably likely contaminant (Food and Drug Administration, 1997a). An FDA study of dried shrimp (Olsen, 1982b) found that the allergenic mites *Dermatophagoides* spp. *S. pontifica* and *T. putrescentiae* may occur in dried shrimp products. A subsequent study found these mites in a wider variety of seafood products (Olsen, 1983). Table 4 lists the allergenic mites that were found as adulterants in seafood products during the 1983 study along with the seafood products in which they were found.

All of the allergenic mites with a proven potential to induce anaphylaxis through ingestion (*cf.* Table 3) occurred as adulterants in seafood samples tabulated in Table 4. These mites were found as adulterants in canned, pickled, and frozen products as well as in dried products. Mites present a challenge to seafood regulators because they are avoidable adulterants. Most other allergenic substances found in seafood are added ingredients or intrinsic components of the product. These added or intrinsic allergens can be controlled through product formulation, label statements, and similar measures that are not applicable to mite adulterants.

The adulteration of seafood with allergenic mites is a result of insanitation. Mites of the families Acaridae, Glycyphagidae, and Pyroglyphidae do not normally oc-

TABLE 4
Allergenic Mites Found as Adulterants in Seafood
(from Olsen, 1983)

Allergenic mite species	Seafood product
<i>Acarus siro</i>	Dried shrimp Dried squid
<i>Dermatophagoides pteronyssinus</i>	Canned crab meat Dried fish Dried shrimp Frozen shrimp Shrimp paste
<i>Euroglyphus maynei</i>	Canned crab meat Dried shrimp
<i>Glycyphagus domesticus</i> <i>Suidasia pontifica</i>	Dried squid Dried fish Dried shark fin Dried shrimp Pickled fish
<i>Thyreophagus entomophagus</i> <i>Tyrophagus putrescentiae</i>	Dried fish Dried fish Dried shark fin Dried shrimp Dried squid

cur in the marine or aquatic habitats from which fish and other seafood are harvested. In nature, many of these mites are nidicoles (inhabiting nests of birds and mammals) (Krantz, 1972). All of the mites listed in Table 4 are pests of stored products that breed in and feed on the products they infest (Hughes, 1976; Smiley, 1991; Olsen and Potter, 1996).

In most cases, infestations of these mites can be avoided or prevented through a sanitation program of the type that is already a prerequisite under the current seafood HACCP regulations (Food and Drug Administration, 1997b). A prerequisite sanitation program that includes regular, effective cleaning of premises and cleaning or sanitizing of equipment and food contact surfaces will remove static material and other harborage for mite pests. Exclusion of birds, rodents, and other pests is an essential precaution to prevent these pests from transporting mites to products or equipment. In addition to infesting seafood, all of the allergenic mites listed in Table 4 may infest nonseafood ingredients such as the spices or flour that are used in the manufacture of pickled or breaded seafood products (Olsen, 1983).

In some cases, allergenic mites may infest a seafood product during processing. As shown in Table 4, mite infestations are most likely to occur in dried seafood products. Large populations of live mites may develop when the drying or curing process requires a long period of time (Olsen, 1982b). Regular inspection of these products during curing or drying and exclusion of other pests such as birds and rodents are often effective in preventing large-scale mite infestations during the processing stage. Manuals for the identification and control of insect and mite pests of dried fish (*e.g.*,

Haines and Rees, 1989) may assist in preventing adulteration from allergenic mites.

CONCLUSIONS

Allergenic mites have been recently identified as an emerging food safety issue by virtue of clinical reports of the discovery that mite allergens may induce anaphylaxis from ingestion of mite-contaminated food. Mite allergens are not intentional food product ingredients or approved food additives, nor are they natural components of any food product. Allergenic mites are avoidable adulterants that may consist, in part, of harmful or deleterious substances (allergens) as defined in section 402(a)(1) of the federal Food, Drug, and Cosmetic Act. As potentially harmful adulterants, allergenic mites are a concern to government agencies responsible for food safety (Pugh, 1996).

Although four species of allergenic mites (Table 3) have been identified thus far as causing IgE-mediated anaphylaxis when ingested, related mite species are known to possess powerful allergens that may, in the future, be demonstrated to induce similar systemic reactions when ingested by sensitized individuals. Based on the available evidence, it is prudent to consider these mites to be a potential food safety issue. Evaluations of adulteration from allergenic mites must take into account the amount of the standard serving portion of a product, as declared on the product's nutritional labeling panel, or the formulation of a product which may contain a mite-infested ingredient in order to determine if an excessive number of mites is likely to be consumed during the normal course of the intended use of a product.

FDA guidance in the area of mite contaminants consists of Compliance Policy Guide 585.500, "Mushrooms, Canned or Dried (Freeze-Dried or Dehydrated)—Adulteration Involving Maggots, Mites, Decomposition," which allows up to 75 mites per 100 g of canned mushrooms or 15 g of dried mushrooms (Michels and Shroff, 1996). These levels, however, are predicated on the assumption that the mite contaminants are harmless and unavoidable. The mite contaminant, *T. putrescentiae*, that induced anaphylaxis in the Matsumoto study is also a common contaminant in mushrooms (Boese, 1981). Individuals who are extremely hypersensitive to mite allergens may be at risk from any level of mite contamination in their food. The true margin of safety for avoiding sensitization or reactions to allergenic mites in food is unknown at this time.

Future research needs include development of methods for direct testing of food products for mite allergens. The capability of direct testing for mite allergens would take into account the allergens present in mite feces as well as those in the bodies of the mites themselves. The most promising candidates in this regard

are the ELISA techniques that have been developed for quantifying the amounts of mite allergens in dust.

It is reasonable to suggest that clinical diagnoses of patients who experience apparent food allergy reactions might include routine screening for sensitivity to allergens from food-contaminating allergenic mites of the families Acaridae s. l., Glycyphagidae, and Pyroglyphidae and testing of suspect food for the presence of allergenic mites and the allergens they produce. In the future, other arthropods may emerge as ingestant allergens in cases of suspected food allergy.

REFERENCES

- Arlian, L. G. (1991). House-dust-mite allergens: A review. *Exp. Appl. Acarol.* **10**, 167–186.
- Arlian, L. G., Bernstein, I. L., Johnson C. L., and Gallagher, J. S. (1979). Ecology of house dust mites and dust allergy. In *Recent Advances in Acarology* (J. Rodriguez, Ed.), pp. 185–195. Academic Press, London.
- Arlian, L. G., Geis, D. P., Vyszynski-Moher, D. L., Bernstein, I. L., and Gallagher, J. S. (1984a). Antigenic and allergenic properties of the storage mite *Tyrophagus putrescentiae*. *J. Allergy Clin. Immunol.* **74**, 166–171.
- Arlian, L. G., Geis, D. P., Vyszynski-Moher, D. L., Bernstein, I. L., and Gallagher, J. S. (1984b). Cross antigenic and allergenic properties of the house dust mite *Dermatophagoides farinae* and the storage mite *Tyrophagus putrescentiae*. *J. Allergy Clin. Immunol.* **74**, 172–179.
- Arlian, L. G., Vyszynski-Moher, D. L., and Fernandez-Caldas, E. (1993). Allergenicity of the mite *Blomia tropicalis*. *J. Allergy Clin. Immunol.* **91**, 1042–1050.
- Armentia, A., and Vega, J. M. (1997). Allergy syndrome after ingestion of salami. *J. Allergy Clin. Immunol.* **100**, 142–143.
- Armentia, A., Martinez, A., Castrodeza, R., Martinez, J., Jimeno, A., Mendez, J., and Stolle, R. (1997). Occupational allergic disease in cereal workers by stored grain pests. *J. Asthma* **34**, 369–378.
- Baldwin, J. L., Chou, A. H., and Solomon, W. R. (1997). Popsicle-induced anaphylaxis due to carmine dye allergy. *Ann. Allergy Asthma Immunol.* **79**, 415–419.
- Beaudouin, E., Kanny, G., Lambert, H., Fremont, S., and Moneret-Vautrin, D. A. (1995). Food anaphylaxis following ingestion of carmine. *Ann. Allergy Asthma Immunol.* **74**, 427–430.
- Bischoff, E. R. C., Fischer, A., and Liebenberg, B. (1992). Assessment of mite numbers: New methods and results. *Exp. Appl. Acarol.* **16**, 1–14.
- Blanco, C., Quiralte, J., Castillo, R., Delgado, J., Arteaga, C., Barber, D., and Carrillo, T. (1997a). Anaphylaxis after ingestion of wheat flour contaminated with mites. *J. Allergy Clin. Immunol.* **99**, 308–313.
- Blanco, C., Castillo, R., Ortega, N., Alvarez, M., Arteaga, C., Barber, C., and Carrillo, T. (1997b). Asthma due to the ingestion of contaminated flour. *J. Invest. Allergol. Clin. Immunol.* **7**, 323–324.
- Boese, J. L. (1981). Mites. In *Principles of Food Analysis for Filth, Decomposition, and Foreign Matter* (J. R. Gorham, Ed.), FDA Tech. Bull. No. 1, pp. 63–82. Food and Drug Administration, Washington, DC.
- Boese, J. L., and Cichowicz, S. M. (1995). Extraneous Materials: Isolation. In *AOAC Official Methods of Analysis*, Chap. 16, pp. 1–69. AOAC International, Arlington, VA.
- Boner, A. L., Richelli, C., Valone, G., Verga, A., Parotelli, R., Andri, L., and Piacentini, G. L. (1989). Skin and serum reactivity to some

- storage mites in children sensitive to *Dermatophagoides pteronyssinus*. *Ann. Allergy* **63**, 82–84.
- Carrillo, T., Rodriguez de Castro, F., Blanco, C., Castillo, R., Quiralte, J., and Cuevas, M. (1994). Anaphylaxis due to limpet ingestion. *Ann. Allergy* **73**, 504–508.
- Castillo, R., Delgado, J., Quiralte, J., Blanco, C., and Carrillo, T. (1996). Food hypersensitivity among adult patients: Epidemiological and clinical aspects. *Allergol. Immunopathol.* **24**(3), 93–97.
- Chapman, M. D., and Platts-Mills, T. A. E. (1978). Measurement of IgG, IgA and IgE antibodies to *Dermatophagoides pteronyssinus* by antigen-binding assay, using a partially purified fraction of mite extract (F4P1). *Clin. Exp. Immunol.* **34**, 126–136.
- Colloff, M. J. (1991). A review of biology and allergenicity of the house-dust mite *Euroglyphus maynei* (Acari: Pyroglyphidae). *Exp. Appl. Acarol.* **11**, 177–198.
- De Maat-Bleeker, F., Akkerdaas, J. H., van Ree, R., and Aalberse, R. C. (1995). Vineyard snail allergy possibly induced by sensitization to house-dust mite (*Dermatophagoides pteronyssinus*). *Allergy* **50**, 438–440.
- Erban, A. M., Rodriguez, J. L., McCullough, J., and Ownby, D. R. (1993). Anaphylaxis after ingestion of beignets contaminated with *Dermatophagoides farinae*. *J. Allergy Clin. Immunol.* **92**, 846–849.
- Evans, G. O. (1992). *Principles of Acarology*. CAB International, Wallingford, UK.
- Food and Drug Administration. (1997a). Fish and fishery products. Title 21, Code of Federal Regulations, **Part 123**, 256–267.
- Food and Drug Administration. (1997b). Sanitation control procedures. Title 21, Code of Federal Regulations, **Section 123.11**, 262.
- Godard, J. (1993). *Physician's Guide to Arthropods of Medical Importance*. CRC Press, Boca Raton, FL.
- Green, W. F., and Woolcock, A. J. (1978). *Tyrophagus putrescentiae*: An allergenically important mite. *Clin. Allergy* **8**, 135–144.
- Guerin, B. (Ed.). (1990). *Mites and Allergic Disease*. Allerbio, Varennes en Argonne, France.
- Guy, C., Dzviga, C., Genot, A., Patural, P., and Ollagnier, M. (1995). Hypersensitivity to Sintrom, caused by cochineal red A. *Therapie* **50**, 483–484.
- Haines, C. P., and Rees, D. P. (1989). *A Field Guide to the Types of Insects and Mites Infesting Cured Fish*, FAO Fisheries Tech. Paper No. 303.
- Hinman, E. H., and Kampmeier, R. H. (1934). Intestinal acariasis due to *Tyroglyphus longior* Gervais. *Am. J. Trop. Med.* **14**, 355–362.
- Hughes, A. M. (1976). *The Mites of Stored Food and Houses*, Ministr. of Agric. Fisheries and Food Tech. Bull. No. 9. Her Majesty's Stationery Office, London, UK.
- Ishi, A. (1975). Researches on the house dust mite in Japan. *Jpn. J. Sanit. Zool.* **26**, 173–179. [In Japanese].
- Kagi, M. K., Wuthrich, B., and Johansson, S. G. O. (1994). Campari-Orange anaphylaxis due to carmine allergy. *Lancet* **344**, 60–61.
- Krantz, G. W. (1972). *A Manual of Acarology*, 2nd ed. Oregon State Univ. Press, Corvallis, OR.
- Lang, J. D., Charlet, L. D., and Mulla, M. S. (1976). Bibliography (1864–1974) of house-dust mites, *Dermatophagoides* spp. (Acarina: Pyroglyphidae) and human allergy. *Sci. Biol. J.* **2**, 62–83.
- Larson, D. G., Mitchell, W. F., and Wharton, W. G. (1969). Preliminary studies on *Dermatophagoides farinae* Hughes, 1961 (Acari) and house dust allergy. *J. Med. Entomol.* **6**, 295–299.
- Liccardi, G., D'Amato, M., and D'Amato, G. (1996). Oral allergy syndrome after ingestion of salami in a subject with monosensitization to mite allergens. *J. Allergy Clin. Immunol.* **98**, 850–852.
- Liccardi, G., and D'Amato, G. (1997). Reply. *J. Allergy Clin. Immunol.* **100**, 143.
- Luczynska, C. M., Griffin, P., Davies, R. J., and Topping, M. D. (1990). Prevalence of specific IgE to storage mites (*A. siro*, *L. destructor* and *T. longior*) in an urban population and cross-reactivity with the house dust mite (*D. pteronyssinus*). *Clin. Exp. Allergy* **20**, 403–406.
- Marcucci, F., Sensi, L. G., and Bizzarri, G. (1985). Specific IgE to food and inhalant allergens in intestinal washings of children affected by atopic eczema. *Clin. Allergy* **15**, 345–354.
- Matsumoto, T., Miike, T., and Ono, T. (1996a). Mite-related allergy and oral tolerance. *Allergy* **51**, 276–277.
- Matsumoto, T., Hisano, T., Hamaguchi, M., and Miike, T. (1996b). Systemic anaphylaxis after eating storage-mite-contaminated food. *Int. Arch. Allergy Immunol.* **109**, 197–200.
- Maunsell, K., Wraith, D. G., and Cunningham, A. M. (1968). Mites and house-dust allergy in bronchial asthma. *Lancet* **June 15**, 1267–1270.
- McDaniel, B. (1979). *How to Know the Mites and Ticks*. Brown, Dubuque, IA.
- Michels, D. L., and Shroff, A. P. (1996). *FDA Compliance Policy Guides*. Food and Drug Administration, Washington, DC.
- Mitchell, W. F., Wharton, G. W., Larson, D. G., and Modic, R. (1969). House dust, mites and insects. *Ann. Allergy* **27**, 93–99.
- Moneret-Vautrin, D. A., and Kanny, G. (1995). Food-induced anaphylaxis. *Bull. Acad. Natl. Med.* **179**, 161–172, 178–184.
- Mulla, M. S., and Medina, M. S. (Eds.) (1980). *Domestic Acari of Colombia: Bionomics, Ecology and Distribution of Allergenic Mites, Their Role in Allergic Diseases*. COLCIENCIAS, Bogota, Colombia.
- Mumcuoglu, Y. (1976). House dust mites in Switzerland. *J. Med. Entomol.* **13**, 361–373.
- Olsen, A. R. (1982a). A new pest of dried fish from the Orient, *Lardoglyphus angelinae* new sp. (Acarina: Acaridae). *J. Stored Prod. Res.* **18**, 181–188.
- Olsen, A. R. (1982b). Mites and other filth in dried shrimp imported into the United States from the Orient. *J. Food Prot.* **45**, 1204–1207.
- Olsen, A. R. (1983). Food-contaminating mites from imported foods entering the United States through southern California. *Int. J. Acarol.* **9**, 189–193.
- Olsen, A. R. (1988). New record of *Lardoglyphus konoi* (Sasa and Asanuma) on dried lizard carcasses. *Pan-Pac. Entomol.* **66**, 126–130.
- Olsen, A. R., and Potter, R. W. (1996). Mites (Arachnida: Acarina). In *Fundamentals of Microanalytical Entomology*. (A. R. Olsen, T. H. Sidebottom, and S. A. Knight, Eds.). CRC Press, Boca Raton, FL.
- Olsen, A. R., Bryce, J. R., Lara, J. R., Madenjian, J. J., Potter, R. W., Reynolds, G. M., and Zimmerman, M. L. (1987). Survey of stored-product and other economic pests in import warehouses in Los Angeles. *J. Econ. Entomol.* **80**, 455–459.
- Platts-Mills, T. A. E., and Carter, M. C. (1997). Asthma and indoor exposure to allergens. *N. Engl. J. Med.* **336**, 1382–1384.
- Platts-Mills, T. A. E., and De Weck, A. L. (1989). Report of an international workshop: Dust mite allergens and asthma: A worldwide problem. *J. Allergy Clin. Immunol.* **83**, 416–427.
- Pollo Corrales, F. (1997). Allergen properties of *Lepidoglyphus destructor*. *J. Invest. Allergol. Clin. Immunol.* **7**, 405–406.
- Potter, R. W., and Olsen, A. R. (1987). Description of a mite *Rhyoglyphus indicus*, new genus, new species, (Acari: Acaridae) found in foods from the Oriental Region. *Int. J. Acarol.* **13**, 271–275.
- Puerta, L., Fernandez-Caldas, E., Lockey, R. F., and Caraballo, L. R. (1993). Sensitization to *Chortoglyphus arcuatus* and *Aleuroglyphus ovatus* in *Dermatophagoides* spp. allergic individuals. *Clin. Exp. Allergy* **23**, 117–123.

- Pugh, S. (1996). Storage mites in foodstuffs. *Food Surv. Inf. Sheet* **96**, 1–5.
- Quirce, S., Cuevas, M., Olaguibel, J. M., and Tabar, A. I. (1994). Occupational asthma and immunological responses induced by inhaled carmine among employees at a factory making natural dyes. *J. Allergy Clin. Immunol.* **93**(Part 1 of 3), 44–52.
- Rosenstreich, D. L., Eggleston, P., Kattan, M., Baker, D., Slavin, R. G., Gergen, P., Mitchell, H., McNiff-Mortimer, K., Lynn, H., Ownby, D., and Malveaux, F. (1997). The role of cockroach allergy and exposure to cockroach allergen in causing morbidity among inner-city children with asthma. *N. Engl. J. Med.* **336**, 1356–1363.
- Sampson, H. A. (1996). Mechanisms of food allergy. *Annu. Rev. Nutr.* **16**, 161–177.
- Sanchez-Borges, M., Capriles-Hulett, A., Fernandez-Caldas, E., Suarez-Chacon, R., Caballero, F., Castillo, S., and Sotillo, E. (1997). Mite-contaminated foods as a cause of anaphylaxis. *J. Allergy Clin. Immunol.* **99**, 738–743.
- Scala, G. (1995). House dust mite ingestion can induce allergic intestinal syndrome. *Allergy* **50**, 517–519.
- Smiley, R. L. (1983). The ordinal and subordinal names of mites with a list of mite pests of stored products. *Proc. Int. Working Conf. Stored-Product Entomol.* **3**, 37–43.
- Smiley, R. L. (1991). Mites (Acari). In *Insect and Mite Pests in Food* (J. R. Gorham, Ed.), Vol. 1, pp. 3–44, Agric. Handbook No. 655. U.S. Dept. Agric., Beltsville, MD.
- Solomon, M. E. (1945). Tyroglyphid mites in stored products: Methods for the study of population density. *Ann. Appl. Biol.* **32**, 71–75.
- Spieksma, F. T. M., and Speiksma-Bozeman, M. I. A. (1967). The mite fauna of house dust with particular reference to the house-dust mite *Dermatophagoides pteronyssinus* (Trouessart, 1897) (Psoroptidae: Sarcoptiformes). *Acarologia* **9**, 226–241.
- Sporick, R., and Platts-Mills, T. A. E. (1992). Epidemiology of dust-mite-related disease. *Exp. Appl. Acarol.* **16**, 141–151.
- Tee, R. D. (1994). Allergy to storage mites. *Clin. Exp. Allergy* **24**, 636–640.
- Tovey, E. R. (1992). Allergen exposure and control. *Exp. Appl. Acarol.* **16**, 181–202.
- Tovey, E. R., Chapman, M. D., Wells, C. W., and Platts-Mills, T. A. E. (1981). The distribution of dust mite allergens in the houses of patients with asthma. *Am. Rev. Respir. Dis.* **124**, 630–635.
- van Bronswijk, J. E. M. H. (1973). *Dermatophagoides pteronyssinus* (Trouessart, 1897) in mattress and floor dust in a temperate climate (Acari: Pyroglyphidae). *J. Med. Entomol.* **10**, 63–70.
- van Hage-Hamsten, M., and Johansson, S. G. O. (1992). Storage mites. *Exp. Appl. Acarol.* **16**, 117–128.
- van Ree, R., Antonicelli, L., Akkerdaas, J. H., Garritani, M. S., Aalberse, R. C., and Bonifazi, F. (1996). Possible induction of food allergy during mite immunotherapy. *Allergy* **51**, 108–113.
- Voorhorst, R., Spieksma-Bozeman, M. I. A., and Spieksma, F. T. M. (1964). Is a mite (*Dermatophagoides* sp.) the producer of the house-dust allergen? *Allergie Asthma* **10**, 329–334.
- Wharton, G. W. (1970). Mites and commercial extracts of house dust. *Science* **167**, 1382–1383.
- Wharton, G. W. (1976). House dust mites. *J. Med. Entomol.* **12**, 577–621.
- Wirtz, R. A. (1984). Allergic and toxic reactions to non-stinging arthropods. *Annu. Rev. Entomol.* **29**, 47–69.
- Woodcock, A. A., and Cunningham, A. M. (1980). The allergenic importance of house dust and storage mites in asthmatics in Brunei, S.E. Asia. *Clin. Allergy* **10**, 609–615.
- Woolley, T. A. (1988). *Acarology: Mites and Human Welfare*. Wiley, NY.
- Wortman, F. (1977). Oral hyposensitization of children with pollinosis or house-dust asthma. *Allergol. Immunopathol.* **5**, 15–26.
- Wraith, D. G., Cunningham, A. M., and Seymour, W. M. (1979). The role and allergenic importance of storage mites in house dust and other environments. *Clin. Allergy* **9**, 545–561.