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The hidden allergens

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One of the main hurdles encountered in the practice of Allergology is that represented by unrecognised substances which may cause sensitization and allergic disease. Such substances could be termed "unknown" or "unreported" allergens, and only after being reported or described will they be incorporated into the diagnostic armamentarium. There is however another type of allergens which, although perfectly known, remain hidden both to the patient and to the allergist, as they are masked or hidden behind other more potent, better known or better foreseeable ones. They thus easily remain unnoticed in the diagnostic process. Over the last few years, the accumulation of new and surprising descriptions of such allergens, which could be termed "masked", "occult" or "hidden", has remarkably increased, and awareness of them is becoming indispensable for all allergists regardless of the level at which they carry out their professional activities.

RESPIRATORY ALLERGY: HIDDEN ALLERGENS IN HOUSE DUST

Beyond the protagonism of the major mites (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*) and of the minor ones, or stora-

ge mites (*Lepidoglyphus destructor*, *Dermatophagoides microceras*, *Eurogliphus mayniei* and *Accarus siro* are just a few of them), further allergens are attaining relevance in "house dust allergy". Thus, in domestic dust the presence of allergens of various *Coleoptera* species has been documented (such as the cockroaches *Blatella germanica* and *Periplaneta americana*). The major allergen in cat epithelia, *Fel dI*, with a great capacity for vehiculation and aerosolisation, is prevalent in the dust collected from households and from public premises such as schools, offices or hospitals never having harboured cats. A recent publication has implicated clothing as the most probable transmission vehicle for this allergen, which will soon have to be considered a major allergenic component in house dust¹. The role of some interior plants, such as *Ficus benjamina*, among others, is also being increasingly considered in the qualitative composition of house dust. The allergens derived from the leaves and stalks of these plants are able to induce both respiratory allergy and contact urticaria.

OCCUPATIONAL ALLERGY: BAKERS' AND GRAIN WORKERS' ASTHMA

Patients exposed to grain (cereals) or to cereal flours are not only exposed to wheat proteins and to the usual parasites, such as mites or moulds. The enzymes added in the course of the processes of bread production, such as α -amylase or cellulase², or the soy added in order to facilitate agglomeration are examples of hidden allergens. Patients exposed to cereals are furthermore also exposed to common cereal parasites, such as the coleoptera *Sitophilus granarius* and *Blatella germanica* or the worm *Tenebrio molitor*³.

FOOD ALLERGY: THE REALM OF THE OCCULT ALLERGENS

Foodstuffs, almost without any exception, are currently exposed to human and industrial manipulation. This facilitates the presence in them of unexpected allergens hidden in various ways⁴. In other cases, however, the problem is one of natural parasitisation, as in the case of the mites parasiting

the flours with which pasta or house-cooked pizzas are prepared⁵, or of worms, such as *Anisakis simplex*, which parasite certain fish species⁶. In these two examples, unawareness of the possible presence of these hidden allergens may lead to incorrect diagnoses and to allergen avoidance measures that are fully unwarranted for those patients.

Proximity contamination of one foodstuff by another one represents one of the most frequent causes of food allergy. There has been quite a volume of reports of allergic reactions caused by the shared use of the same table or kitchen utensils or of the same frying oils, or by unnoticed quantities of an allergenic foodstuff present yet not visible in a prepared food. The use of latex gloves in the preparation of sandwiches in company or public cafeterias has led to unexplainable allergic reactions in patients sensitized to that allergen. Spices, and particularly the most commonly used ones such as pepper or mustard, may remain unnoticed even for the most careful patients, and will cause confusion in the diagnosis of food allergy. Sesame, an Oriental spice that has been recently introduced in the Occidental diet in sauces or vegetarian cooking, but also in the exotic foods consumed during trips to foreign countries, contains potent allergens and is responsible for quite a number of severe allergic reactions⁷. A further possibility that should not be forgotten is that of food allergy caused by the ingestion of enzymes added to foodstuffs, such as α -amylase, lactase or papain.

The composition specifications and rulings for manufactured foodstuffs hide further surprises: "milk-free" desserts that contain lactalbumin, "wheat-free" cereal flours reinforced with gluten, or the frequent presence of peanut or soy in all variants of alimentary products⁸ are excellent examples of hidden or masked allergens. The growing power of the alimentary industry and the professional secret lead to equivocal labelling in which designations such as "emulgent", "lecithin", "gelatin" or "natural dyes" hide such dangerous allergens as ovoalbumin, soy, animal proteins or carmine, with dire consequences for the allergic patient. The formulations "imitation..." or "substitute..." represent a considerable risk for patients with food allergy.

Occasionally, the occult factor leading to the diagnostic error is not properly an allergen, but a second factor which masks the aetiology of the

reaction. This is the case in anaphylaxis through exertion-associated food allergy, reported already in relation to dozens of foodstuffs, in which the diagnosis can only be established when the patient is questioned about the relationship between physical exertion and the ingestion of the possible foodstuff involved. In other cases, accidental warming or prolonged storage of foodstuffs containing proteins together with high carbohydrate concentrations may give rise to the formation of neoallergens (the Maillard effect). Finally, the irruption of the modern alimentary technology and the generation of transgenic foodstuffs generate the most effective "masking costume" for occult allergens: their insertion into the genetic code of another foodstuff⁹. This virtual possibility has become real indeed in the case of patients who are allergic to Brazil (or cashew) nut, in whom positive skin tests and specific IgE have been demonstrated to a certain type of transgenic soy, in the genetic code of which genes coding for allergenic proteins (2S albumin) of Brazil nut had been inserted¹⁰.

HIDDEN ALLERGENS IN DIAGNOSTIC METHODS

The inadvertent presence of acarine allergens (*Der pI*) in dog epithelia extracts used for skin testing may be the cause of mistaken diagnoses of allergy to dog epithelia in patients with dust mite allergy¹¹. Obviously, in this case the removal of the dog from the household will represent no therapeutic benefit for the patient. Similarly, the presence of carboxymethylcellulose or seaweed derivatives in barium salt preparations should be investigated in the case of patients developing allergic reactions after diagnostic procedures in which barium meals or barium enemas had been used.

THERAPEUTICS AND OCCULT ALLERGENS

In the decade of the '70s, a number of drugs which were commonly used in anaesthesia had to be retired from the market because of frequent anaphylactoid accidents, some of them with fatal results. Later investigations identified the agent

responsible for these severe reactions: the solvent Cremophor-EL, consisting of polyoxyethylated castor oil. In spite of these accidents, castor oil remains in use in both oral and parenteral preparations, and has recently been again incriminated as the causative agent in cyclosporin allergy¹². Other compounds, such as carboxymethylcellulose or gum arabic, have emerged as causative agents in cases of allergy to some preparations, for instance parenteral corticosteroids or thyroid hormone tablets.

The prophylactic therapy agents *par excellence*, that is, vaccines, are not exempt from the invasion by occult allergens. Besides ovoalbumin, present at picogram concentrations, gelatins of both bovine and porcine origin are also present in vials of virus vaccines in concentrations as high as 10 mg/vial and are responsible for a considerable number of allergic reactions to such vaccines. Furthermore, the presence of these gelatins in sweets and soft candies that are frequently consumed by children favours the apparition of cross-reactivity reactions¹³.

The realm of occult, hidden or masked allergens appears to be experiencing a disproportionate growth. And yet, this phenomenon is but beginning: over the coming years we shall witness the discovery of many and highly variegated occult allergens, and this will beyond any doubt clarify many complex or intricate diagnoses and benefit many patients. Only if these possibilities are recognised and if we remain attentive and aware to the new discoveries shall we be able to respond to this peculiar diagnostic challenge.

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