

Meat allergy

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Purpose of review

This review summarizes the scientific evidence on meat allergy, an unusual disorder, whose prevalence in some European countries (such as Italy) may be increasing.

Recent findings

Data reported in this review underline some interesting points: in meats rarely consumed, such as kangaroo, whale and seal, the main allergens are only partially correlated to those detected in beef or other usually consumed meats; cross-reactivity and cross-contamination are critical aspects, which should be seriously considered by allergologists.

Summary

Meat allergy is normally outgrown during the first years of life, so that it is rare in adults. Beef among mammals and chicken among birds are most frequently involved. The major allergens are serum albumins and immunoglobulins, but there are a few reports of allergies to muscle proteins (actin, myosin and tropomyosin). As meat allergenicity can be reduced by various treatments (heat, homogenization and freeze-drying), the consumption of meat derivatives by children allergic to meat proteins is often permitted. Cross-reactivity has been described between different meats, between meat and milk or eggs and between meat and animal dander. There are some reports of cross-contamination associated with the inadequate cleaning of industrial or butchers' equipment. All these aspects may have serious implications for clinical practice.

Keywords

cross-contamination, cross-reactivity, immunoglobulins, meat allergy, serum albumins

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Introduction

Meat allergy is rare, especially in adults; meat allergy presenting in infancy is usually outgrown during the first years of life [1]. The study by Fuentes Aparicio *et al.* [1] describes one of the rare cases of meat allergy in adult life. The observed IgE-mediated urticaria–angioedema was associated with BSA hypersensitivity possibly induced by a subclinical sensitivity to dog and cat epithelium. Meat allergy's frequency is controversial both with regard to the number of allergic patients and the type of meat involved. The prevalence varies with geographical area [2,3^{••}], and local diet is important for the development of specific sensitizations such as the allergy to kangaroo in Australia [4] or to seal and whale meat in Alaska [5^{••}]. Allergy to avian meat is even rarer and is normally not correlated with an allergy to mammalian meat. The prevalence of beef allergy (the most frequent meat allergy), evaluated by double-blind placebo-controlled food challenge (DBPCFC), ranges between 1.5 and 6.5% in children suffering from atopic dermatitis or food allergies/intolerances [6–8]. The prevalence can be as high as 20% in children allergic to cow's milk [8].

Nutritional value of meat proteins

Meat is usually defined as the flesh and organs of animals (mammals, reptiles or amphibians) and birds (mainly poultry). Meat is not essential for an adequate diet, but it provides proteins of high biological value and important micronutrients involved in good health status. Lean meats contain approximately 20% of proteins providing all essential amino acids. Dietary meat is more important for children and adolescents than in adults as meat reduces the risk of iron-deficiency anemia, which can have serious, often irreversible, adverse outcomes including physical, neurological and psychomotor abnormalities [9^{••}]. For these reasons, inclusion of meat is usually recommended in the diet of young children, and in particular during the weaning period [10,11]. On these bases, meat allergy can alter significantly the nutritional value of the diet during the weaning period.

Meat allergens

As meat allergy is infrequent, molecular studies of the condition are limited, and only a few proteins have been

Table 1 Meat allergens present in the list of the Allergen Nomenclature Sub-Committee of the International Union of Immunological Societies

Species (common name)	Species (latin name)	Allergen name	Biochemical name	Molecular weight (kDa)
Cow	<i>Bos domesticus</i>	Bos d 6	Serum albumin	67
Cow	<i>Bos domesticus</i>	Bos d 7	Immunoglobulin	160
Chicken	<i>Gallus domesticus</i>	Gal d 5	Serum albumin	69

Data from Allergen Nomenclature Sub-Committee of the International Union of Immunological Societies [12].

identified as major allergens. In the official list of food allergens [12], there are only three meat proteins (Table 1) – two serum albumins and bovine immunoglobulins. Other serum albumins, not included in the official list of allergens, have been associated with allergy to other mammalian species such as pork [13–16], lamb [16] and rabbit [16]. Additional proteins have been indicated as major or minor allergens in meats, although their precise identification was uncertain (Table 2) [17–20]. Table 2 shows that the proteins from very different animal species, immunodetected by specific IgEs from meat allergic patients, have similar electrophoretic properties. Results from different studies show that:

- (1) whale, seal, kangaroo and turkey contain a reacting protein of molecular weight 80–90 kDa;
- (2) whale, chicken and turkey do not contain the 30–40 kDa molecular weight reactive protein(s);
- (3) the 20–25 kDa bands might represent the light chain of immunoglobulins;
- (4) the 45–50 kDa bands might represent the heavy chain of immunoglobulins; and
- (5) the 38–40 kDa bands might represent actin [21].

The clinical significance of in-vitro immunoreactivity of actin is doubtful, because for several studies [7,21], the positive reactions were not confirmed by skin prick test (SPT) and/or oral challenge. This could be explained by a difference in allergenicity between polymerized actin in meat and monomers utilized in in-vitro tests. The muscle protein tropomyosin, which is the main allergen in crustacean species, seems to play a minor role in mammalian and avian meat allergy [22,23].

A very recent study [24**] reports the identification of 24 patients who reported no oral allergy syndrome-type

clinical reaction but experienced delayed systemic symptoms (3–6 h) associated with eating beef, pork or lamb. These patients showed the following diagnostic pattern: very high titer of specific IgE to beef, pork, lamb and cow's milk; wheal diameter to SPT commercial extracts lower than 4 mm; larger wheal diameter when beef, pork and lamb extracts from fresh meat were used. This 'anomalous' group of patients showed detectable IgE antibodies to galactose- α -1,3-galactose (α -gal). α -gal epitope is abundantly expressed on cells and tissues of nonprimate mammals, and it is involved in the IgG-mediated hyperacute rejection of pig-to-primate xero-transplantation. Two main points are still open regarding this novel pattern of meat allergy: the reasons why the reactions are delayed for several hours, and the events responsible for the production of IgE antibodies to α -gal.

Destruction by cooking and technological treatment

The allergenicity of foods can be modified by domestic or industrial processing; enhanced, decreased or unaffected antigenic reactivity has been reported. The molecular changes involved in modifying the allergenic potential can be summarized as follows: heating or other treatments can modify or inactivate the epitopic domains responsible for the IgE binding by changing the conformation of the epitopes; or denaturation of the three-dimensional structure of a protein can produce new epitopes and enhance the accessibility of the allergenic determinant to specific antibodies.

Cooking often modifies or destroys heat-labile allergens, but some patients will still react to cooked foods as shown by a useful review by Fiocchi *et al.* [23]. Very few data have been published on the relative stability of different

Table 2 Molecular weight (kDa) of proteins included or not included in the official list of allergens that have been indicated as major or minor meat allergens

Range (kDa)	Beef/veal	Pork	Kangaroo	Seal	Whale	Chicken	Turkey
81–100			81	90	90		91
61–80	66.4 ^a	66.8				67.2 ^a	
45–60	45	51		50	55	50	50
31–44	38	40	41	40			
20–30	21	28–30		25		21, 23	21, 23
[Ref.]	[17]	[18,19]	[4]	[5**]	[5**]	[20]	[20]

^a Serum albumins (included in the official list of allergens).

meat allergens. Cases of adverse reaction to raw meat coupled with tolerance to well cooked beef have been described, as judged by SPT [25], IgE binding [8,17] or oral challenge [11,26], and similar results were found with raw and cooked chicken meat [26].

Homogenization and freeze-drying, industrial processes usually applied to meat during the production of baby-foods, can significantly decrease the allergenic potential of beef [27]: raw beef, domestically cooked beef (100°C for 5 min) and unheated BSA elicited a positive SPT response in a group of 12 children with clinically documented beef allergy, whereas homogenized and freeze-dried beef preparations did not. In oral challenges, all the children reacted to home-cooked beef and some of them to heated BSA, but there was no clinical reaction to either homogenized or freeze-dried beef. Thus, home cooking may be insufficient to affect the complex matrix of meat and the associated blood albumins and immunoglobulins, whereas it was shown that the industrial processes decrease the content of these proteins [28].

Cross-reactivity

There are three different types of cross-reactions in patients suffering from meat allergy: between meats from different animal species; between meat and other foods; and between meat and animal dander.

Cross-reactivity between meats from different animal species

The probability of cross-reaction is high if the animals are phylogenetically similar. Patients allergic to beef may

react to sheep and pork but not to avian meats. Similarly, patients reactive to chicken usually cannot eat turkey but tolerate mammalian meats [28]. This relationship of cross-reactivity to phylogenesis has been well documented by investigating one of the major meat allergens, serum albumin [21].

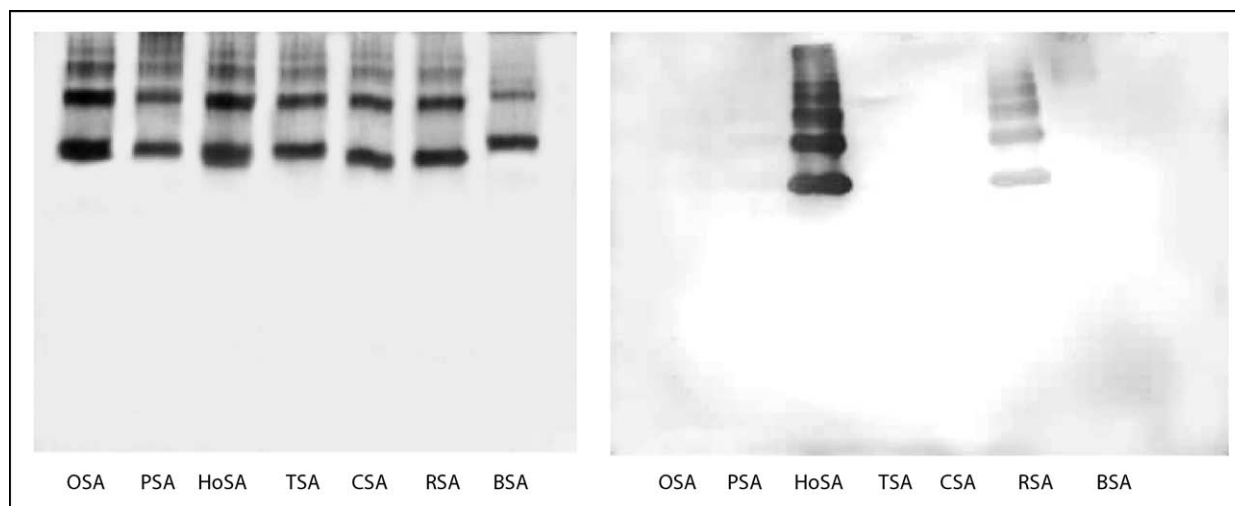
Cross-reactivity between meats and other foods

The clinical reaction to milk in patients allergic to mammalian meat is well known and occurs in a high percentage of these patients; in two studies performed by DBPCFC, 73 [17] and 93% [29] of children allergic to beef were also clinically reactive to cow's milk. The sensitivity to BSA was the main predictive marker of cow's milk allergy in children with beef allergy [29]. Patients allergic to chicken can experience reactions to egg, and chicken serum albumin is responsible for the double intolerance, as it is closely homologous to egg α -livetins [26].

Cross-reactivity between meats and corresponding animal dander

Several cases of meat allergy in patients suffering from IgE-mediated reactions (mainly urticaria–angioedema) due to subclinical or clinical sensitivity to an animal's epithelium have been reported. In some of these cases, immunoblotting and immunodot studies showed that IgE binding to bovine and lamb meat proteins was totally inhibited by BSA, showing the role of this allergen in the phenomenon of cross-reactivity [1]. Our group encountered a case (unpublished) of cross-reactivity between meat and an animal's epithelium in 1995 when an 8-year-old girl suffering from severe allergic symptoms, including asthma, arrived at the emergency department.

Figure 1 SDS-PAGE of serum albumins (left) and immunoblotting obtained by incubating the corresponding membrane with the serum of the girl sensitized to horse and rabbit epithelia (right)



BSA, bovine serum albumin; CSA, chicken serum albumin; HoSA, horse serum albumin; OSA, ovine serum albumin; PSA, pork serum albumin; RSA, rabbit serum albumin; TSA, turkey serum albumin.

According to the usual diagnostic tests [SPT and radio-allergosorbent test (RAST)], she was sensitized to horse and rabbit epithelium, and she stopped the horse riding she had begun some months before. A year later, she unknowingly consumed a meal containing horse meat and experienced an anaphylactic shock requiring hospitalization. The results of an immunoblotting test using the child's serum are shown in Fig. 1. There was a specific reaction to horse and rabbit serum albumins but none to serum albumins from other animal species. A further immunoblotting test using meat proteins from different animal species (not shown) confirmed the involvement of serum albumins in cross-reactivity between horse meat and the animal's shed epithelial cells.

Cross-contamination

Cross-contamination is a well known problem in the food industry: when the same equipment is used for processing different foods, traces of unsuspected ingredients can remain. Several guidelines have been published aimed at reducing cross-contamination; particular atten-

tion has been paid to milk and eggs, which are ingredients widely used in food preparation.

We describe here another unpublished clinical case registered in 2004: a child allergic to beef, cow's milk and eggs experienced severe urticaria and angioedema after consuming a chicken/pork hamburger prepared by a butcher who was acquainted with the child's disease and who prepared for the child every week several hamburgers using the same mixture of meats. Using a specific antibody developed against BSA, we were able to explain the clinical reaction to the hamburgers, which were normally well tolerated. Figure 2 shows that an immunoreactive band, absent from the tolerated meats (chicken and pork), was evident both in beef and the prepared hamburger. This result showed unequivocally the presence of bovine meat in the hamburger. The 'accident' was probably due to a busy period for the butcher who had forgotten to perform the cleaning steps necessary to ensure the elimination of previous meats from the chopping machine.

Conclusion

Meat allergy is generally considered to be rare, but its prevalence in children of some European countries, including Italy, is significant. Apart from identifying the allergen, the allergologist must take into account different patterns of cross-reactivity when the diet of meat-allergic children is formulated. Sensitization to animal dander (sloughed epithelial cells) enhances the probability that animal meat allergy will develop. Guidelines are important in the control of cross-contamination in industrial food processing and for retailers, who need to be aware of the possibly tragic consequences for allergic children when careful cleaning of equipment is skimmed.

References and recommended reading

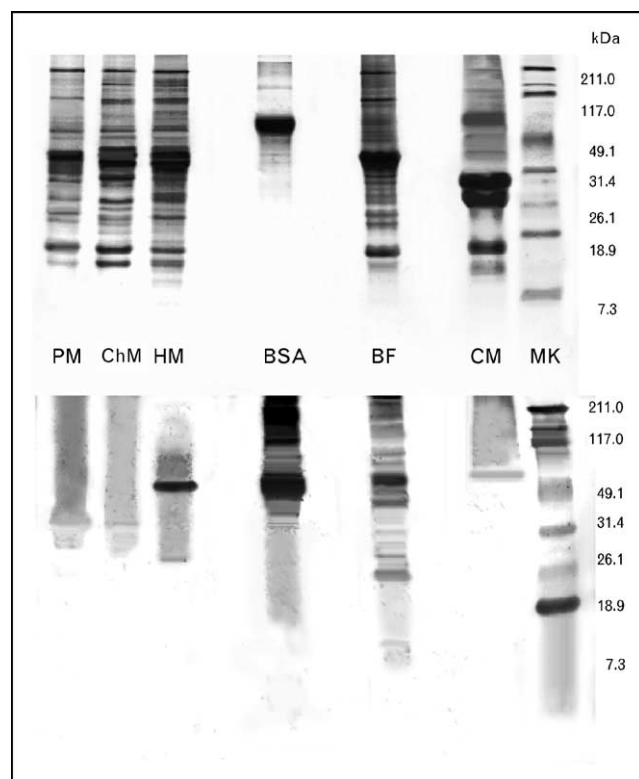
Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 000–000).

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Figure 2 SDS-PAGE of meats from different animal species and BSAs (above) and immunoblotting obtained by incubating the corresponding membrane with the serum of the child experiencing clinical symptoms after the consumption of a 'contaminated' hamburger (below)



BF, beef; ChM, chicken meat; CM, cow's milk; HM, contaminated hamburger; MK, molecular weight standard solution; PM, pork meat.

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