Allergy to meats

Author: Scott P Commins, MD, PhD
Section Editor: Scott H Sicherer, MD, FAAAAI
Deputy Editor: Anna M Feldweg, MD

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Literature review current through: Feb 2021. | **This topic last updated:** Jan 28, 2020.

INTRODUCTION

Meat allergy is uncommon in the developed world, despite relatively high levels of meat consumption [1]. Childhood meat allergy is usually associated with atopic dermatitis and outgrown during the first years of life. Meat allergy can also develop in adulthood.

The epidemiology, clinical manifestations, diagnosis, and natural history of allergy to meats will be discussed in this topic review. Fish and seafood allergies are mentioned briefly here and discussed in greater detail elsewhere. General issues related to food allergies are presented separately.

- (See "Seafood allergies: Fish and shellfish".)
- (See "Clinical manifestations of food allergy: An overview".)
- (See "History and physical examination in the patient with possible food allergy".)
- (See "Diagnostic evaluation of food allergy".)

EPIDEMIOLOGY

Meat allergy is relatively uncommon, although the overall incidence and prevalence of allergies to meat in the general population are not known. Among patients with food allergies, meat allergy has been reported in about 3 to 15 percent of pediatric cases [2,3] and 3 percent of adult cases [4]. The low prevalence of meat allergy may be in part attributable to the fact that most meats are eaten in cooked forms, and cooking usually (not always) reduces the immunogenicity of allergens. (See 'Allergens' below.)

CAUSATIVE MEATS

The type of meats that cause allergy appear to be related to their prominence in the diet, and geographic variations are evident [5,6].

Beef is the most commonly reported allergy, with a prevalence of beef allergy ranging from 1.5 to 6.5 percent among children with atopic dermatitis or food allergies/intolerances [1,7,8]. However, the prevalence of beef allergy can be as high as 20 percent in children allergic to cow's milk [1]. (See 'Patterns of cross-reactivity' below.)

Allergic reactions to pork, lamb, rabbit, chicken, and turkey are also reported [9-11]. Case reports describe allergies to kangaroo meat in Australia, as well as seal and whale meats in native Alaskan populations [12,13]. Overall, allergy to mammalian meats is more prevalent than allergy to poultry.

Risk factors — Risk factors for the development of allergy to meats have not been fully defined and may be different depending on the allergen to which the patient is sensitized:

- Growing evidence suggests that multiple tick bites may be a risk factor for allergy to nonprimate mammalian meats. (See 'The role of ticks in red meat allergy' below.)

- An association between blood groups A and O and sensitization to galactose-alpha-1,3-galactose (alpha-gal) has been noted [14,15].
- Children with atopic dermatitis or cow's milk allergy may be at increased risk, based on earlier epidemiologic studies [1,7].
- Patients with gelatin allergy may also be sensitized or clinically reactive to meats [16].

The allergens involved in meat allergy are discussed in more detail below. (See 'Allergens' below.)

The role of ticks in red meat allergy — In susceptible individuals, multiple tick bites appear to result in sensitization to the carbohydrate allergen alpha-gal, which is present in many mammalian meats [17]. (See 'Alpha-gal' below.)

Meat allergy caused by alpha-gal sensitization has been reported in several parts of the world, including the United States, Australia, Spain, Germany, Japan, and Sweden [18-21]. Alpha-gal is present in the gastrointestinal tract of at least one species of tick [22], and many of the patients described have reported that allergic symptoms to meat ingestion began after a series of tick bites. Thus, it is possible that some patients become sensitized as a result of tick bites, as stomach contents are regurgitated into the skin during the attachment process. The tick species most often implicated in meat allergy have been *Amblyomma americanum* (ie, the lone star tick) (picture 1) in the southeastern United States and other species (*Ixodes ricinus, Ixodes holocyclus, Amblyomma cajennense, Amblyomma sculptum,* and *Haemaphysalis longicornis*) in other parts of the world [22-24].

CLINICAL REACTIONS

Both immunoglobulin E (IgE)-mediated and non-IgE-mediated forms of meat allergy have been described.

IgE-mediated reactions — Children with meat allergy often have atopic dermatitis and present with exacerbations of skin inflammation following ingestion of certain meats [25], although they can also develop other symptoms, such as pruritus, urticaria, or even asthma [7]. (See "Role of allergy in atopic dermatitis (eczema)", section on 'Food allergies'.)

In adults, skin symptoms are also common during allergic reactions to meat. One series of 10 patients with symptoms beginning in adulthood reported that the most common symptoms after meat and milk ingestion were cutaneous pruritus and/or urticaria (70 percent), followed by gastrointestinal symptoms (40 percent) [26]. Other responses included contact urticaria of the oral mucosa (oral allergy syndrome) and anaphylaxis. These 10 patients developed symptoms after ingestion, but not in response to contact or inhalational exposures. All 10 patients had specific IgE to one or more meats or milk upon serologic testing.

One unusual feature of IgE-mediated allergic reactions to meat caused by galactose-alpha-1,3-galactose (alpha-gal) is that symptoms can be relatively delayed in onset. In patients with convincing evidence of IgE-mediated allergy, reactions began as quickly as several minutes or as delayed as three to six hours after ingestion [18,19,27]. Patients may develop symptoms in the middle of the night after eating meat for dinner. This disparity in time to symptoms may be explained by the nature of the allergen (ie, protein versus carbohydrate). (See 'Alpha-gal' below.)

Allergens — Limited information is available about the allergens responsible for IgE-mediated meat-allergic reactions [28]. Both protein and carbohydrate allergens have been identified.

Serum proteins — Serum albumins and immunoglobulins appear to be the primary allergenic proteins in beef and other mammalian meats [11,29]. Albumins have been implicated in allergies to beef, pork, lamb, and rabbit, as well as chicken [9-11,29,30]. The International Union of Immunological Societies lists just three meat proteins in its official listing of important food allergens. Two of bovine origin (a serum albumin, Bos d 6 and an immunoglobulin, Bos d 7) and one from chicken (serum albumin) [31]. (See "Food allergens: Overview of clinical features and cross-reactivity" and "Molecular features of food allergens".)

Sequence homology between bovine serum albumin (BSA) and pig, sheep, and chicken serum albumins were 80, 92, and 44, respectively, supporting the clinical observation that individuals tend to react to mammalian meats or poultry but rarely both [32-34]. Cross-reactivity between beef and whey proteins from milk has been attributed to serum albumins and gamma-immunoglobulin [28]. (See 'Meats and other foods' below.)

The low prevalence of meat allergy may be in part attributable to the heat labile properties of serum albumins and the fact that most meats are eaten in cooked forms.

Additional proteins in meat that may act as major and minor allergens have been identified [11-13,29,34-36]. As an example, denatured type I bovine collagen has been identified as the major allergenic component of bovine gelatin [37]. The clinical significance of some meat allergens is not known. These proteins are diverse and likely represent light chain immunoglobulins, heavy chain immunoglobulins, and muscle proteins, such as actin.

Alpha-gal — Although most known food allergens are proteins, carbohydrate epitopes, bound to either protein or lipid molecules, can also act as allergens. The carbohydrate moiety galactose-alpha-1,3-galactose (alpha-gal) is abundantly expressed on cells and tissues of all mammalian species **except** primate mammals (ie, humans, chimpanzees, and old world monkeys). Patients sensitized to alpha-gal report delayed symptoms to a wide range of mammalian meats, especially beef, pork, and lamb [18]. They can also react to organ meats (ie, kidney), gelatins in foods and candies, and milk [16,38,39]. Patients with allergies to gelatins and milk can be sensitized to allergens other than alpha-gal and require further evaluation if mammalian meat is clearly tolerated.

The IgE response to alpha-gal has been found in both adults and children [40-43]. Most patients in an early report had urticaria, angioedema, or anaphylaxis, although a few individuals had gastrointestinal symptoms accompanied by presyncope or syncope without urticaria or angioedema, a presentation that is more difficult to recognize as an allergic reaction. The onset of symptoms was significantly later compared with typical IgE-mediated reactions, beginning three to six hours after ingestion. The authors of the study mentioned above identified IgE to alpha-gal in 1 to 3 percent of the population in selected areas of the southern, central, and eastern United States, although there are not formal studies of prevalence [44]. Similar patients have been reported in Europe, Asia, and Australia [15,19-21,45-49].

The delayed onset of symptoms may be related to binding of the alpha-gal allergen to lipids, which are absorbed more slowly and by different mechanisms compared with proteins. An in vitro model found that only alpha-gal bound to lipids was able to cross a monolayer of intestinal epithelial cells and activate basophils from a patient with alpha-gal allergy [50].

In addition to reacting to foods, patients sensitized to alpha-gal may also have reactions to the monoclonal antibody cetuximab, gelatin administered in vaccines [40,51], vaginal capsules [52], or intravenous colloids [53], heparin [54], bovine or porcine heart valves [54], and possibly other hemostatic agents derived from animal products. Cross-reactivity with the medication cetuximab is discussed below (see 'Meats and monoclonal antibodies (cetuximab)' below). Alpha-gal-related reactions to vaccines, heart valves, hemostatic agents, and colloids are discussed in more detail separately. (See "Allergic reactions to vaccines", section on 'Gelatin' and "Perioperative anaphylaxis: Clinical manifestations, etiology, and management", section on 'Role of alpha-gal allergy'.)

Role of cooking — Domestic or industrial processing can alter the allergenicity of foods by modifying or inactivating the epitopes for IgE binding. In most cases (not all), this results in no change [55] or decreased reactivity [1,27,29,32], and this is probably true for meat allergens, as well. (See "Pathogenesis of food allergy" and "Molecular features of food allergens", section on 'Protein stability'.)

Other forms of processing, such as homogenization or freeze drying, can also alter allergenicity. A study of 12 children with clinically documented beef allergy found that all of the children reacted to home-cooked beef during oral challenges and some of them reacted to heated BSA [56]. However, none reacted to either homogenized or freeze-dried beef (the industrial processes that are usually used in the production of baby foods). Homogenization and/or freeze drying have been shown to decrease the content of blood albumins and immunoglobulins (eg, the primary allergenic proteins) in meat. Digestion with pepsin was also shown to nearly eliminate allergenicity for most patients.

Eosinophilic esophagitis — Eosinophilic esophagitis (EE) typically presents with symptoms of gastroesophageal reflux unresponsive to acid suppression and dysphagia for solids, especially in young men or boys. The majority of patients (90 percent) are sensitized to both food and aeroallergens, yet only 10 to 30 percent have a history of food anaphylaxis [57]. The diagnosis is based on the presence of characteristic clinical features, a large number of eosinophils on esophageal biopsy, and the exclusion of other causes. The pathogenesis of EE is believed to involve both IgE-mediated and non-IgE-mediated hypersensitivity. (See "Clinical manifestations and diagnosis of eosinophilic esophagitis" and "Treatment of eosinophilic esophagitis".)

Beef, chicken, and cow's milk have been implicated as causing esophageal inflammation in patients with EE. Patients typically develop symptoms in response to more than one food. In one study, an average of three to six problematic foods per patient were identified [57]. The foods most often implicated were milk, egg, soy, chicken, wheat, beef, corn, and peanuts [58].

Food protein-induced enterocolitis syndrome — Food protein-induced enterocolitis syndrome (FPIES) represents a non-IgE-mediated form of food allergy that usually presents in infants [8,56]. Symptoms of typical FPIES are delayed by a median of two hours and include vomiting, diarrhea, and lethargy/dehydration [59]. Bloody diarrhea may be present, and infants are generally ill-appearing. (See "Food protein-induced allergic proctocolitis of infancy".)

Although cow's milk and soy protein are the most common triggers, FPIES can be triggered by other proteins, including beef, chicken, and turkey [60]. The author is not aware of published reports of enterocolitis caused by meats beginning in adulthood.

PATTERNS OF CROSS-REACTIVITY

Several clinical syndromes have been described that involve cross-reactivity or cross-sensitization between meat allergens and other types of allergens.

Meats from different animal species — The probability of cross-reactivity is increased the more closely related the animals are evolutionarily [34]. Patients allergic to beef may react to mutton or pork but rarely to poultry or fish. Similarly, patients may react to chicken and turkey but not to mammalian meats [11]. Cross-reactivity among goose, duck, turkey, and chicken meat has been demonstrated [61]. In many cases, cross-reactivity has been shown to be due to immunoglobulin E (IgE) specific for common determinants on serum albumins [36]. (See 'Allergens' above.)

Fish/chicken allergy — Patients have been described who are allergic to chicken meat (but not hen's egg) and to fish, due to sensitization to cross-reactive parvalbumins, enolases, and aldolases [62].

Meats and other foods — The following observations have been made about cross-reactivity between meats and other animal-derived foods:

- Beef and cow's milk – Allergy to cow's milk is present in 73 to 93 percent of beef-allergic patients, most of whom are children [31,61]. Sensitization to bovine serum albumin (BSA) is the main predictive marker of this cross-reactivity [61]. Milk allergy is reviewed in more detail separately. (See "Milk allergy: Clinical features and diagnosis" and "Milk allergy: Management".)

- Beef and beef gelatin – Allergy to beef gelatin is seen in some patients with allergy to beef. The responsible allergen may be galactose-alpha-1,3-galactose (alpha-gal) [16]. Patients with gelatin allergy may report reactions to vaccines or foods that do not contain obvious meats. (See "Allergic reactions to vaccines", section on 'Gelatin'.)

On the other hand, patients with a meat allergy may not react to other foods/inhalants derived from the same animal source. As examples:

- Anaphylaxis due to ingestion of porcine gut and kidney, with tolerance of pork meat, has been described [35]. This patient also reacted to lamb gut. This case illustrates that allergens can be tissue-specific.

- Adults have been described who are allergic to poultry meat but tolerant of eggs and not allergic to poultry feathers or dander [11,63]. The responsible allergen(s) have not been identified, although they are likely different from the allergens that cause bird-egg syndrome. (See 'Meats and animal dander/epithelium' below.)

Meats and animal dander/epithelium — Patients allergic to meats may show cross-reactivity with animal epithelia or dander. The following have been reported:

Bird/egg allergy — "Bird-egg syndrome" is a term used to describe adults with allergic respiratory disease provoked by the inhalation of bird feathers or dander, who also develop allergic symptoms with hen's egg ingestion [64]. Alpha livetin (also known as chicken serum albumin, Gal d 5) found in the dander and yolk proteins of chicken egg is the major allergen

responsible for these reactions [65-67]. This allergen is also present in chicken meat, but only a minority of patients with bird feather allergy report chicken meat allergy, most likely because the allergen is altered by cooking [68].

Pork/cat allergy — Cross-reactivity between cat epithelia and pork meat due to homologous serum albumins also exists [69-71]. A case of fatal anaphylaxis was described in a patient who had known allergy to pork and ingested wild boar meat [72]. This patient was also sensitized to cat albumin (Fel d 2), which is now a commercially orderable IgE test. The term "pork-cat syndrome" was coined by the group who reported this case. Sensitization to cat serum albumin was also demonstrated in a series of eight patients from the United States [71]. The reactions to pork began soon (within two hours) after ingestion, distinguishing this syndrome from allergy to carbohydrate allergens. Of note, patients with pork-cat syndrome may **not** have allergic rhinitis symptoms to cat dander. Most patients with allergic symptoms to cat dander are sensitized to a different allergen (Fel d 1).

Horse meat/horse dander allergy — Cross-reactivity between horse meat and horse epithelium was demonstrated in a young female who was sensitized to horse epithelium and experienced anaphylaxis after unknowingly eating a meal with horse meat [27].

Meats and monoclonal antibodies (cetuximab) — The cross-reactive carbohydrate determinant, alpha-gal, which is present on a range of mammalian meats, has been shown to be a potent allergen [18]. Patients who have IgE to alpha-gal can develop severe hypersensitivity reactions to the monoclonal antibody cetuximab, which also contains alpha-gal [73]. This association was made after a group of patients experienced anaphylaxis upon their initial exposure to cetuximab, indicating that they had been previously sensitized to some component of the drug. A subset of these patients living in the southeastern United States described delayed anaphylaxis to beef, pork, or lamb, despite having tolerated these meats previously. These reactions are atypical for IgE-mediated allergy in that they do not start until several hours after meat ingestion and are associated with negative or very weak wheal responses to prick tests with meat extracts [18]. (See 'Alpha-gal' above and 'Diagnosis' below.)

DIAGNOSIS

The diagnosis of meat allergy can be challenging. Several studies have described poor correlation between the clinical history, skin test results, immunoassays to food-specific immunoglobulin E (IgE), and outcomes of food challenges [1,28,74-76]:

- One series described 13 patients with convincing clinical histories of chicken, beef, or pork allergy [74]. Three had life-threatening reactions and positive skin tests to the suspect meat and so were not challenged, but the remaining 10 underwent a double-blind placebo-controlled food challenge (DBPCFC) with up to 50 grams of well-cooked meat. Only 3 of the 10 challenged patients reacted to challenge. However, other beef challenge protocols have identified positive reactions at higher doses, such as 75 grams. Thus, meat allergy was confirmed in 6 of 13 patients. Just one of the challenge-positive individuals had positive skin tests to a commercial extract of the suspect meat. Two patients had demonstrable meat-specific IgE (by ImmunoCAP testing). Five of the seven patients with a **negative** challenge test showed evidence of specific IgE to the suspect meat, either by skin testing or immunoassay, reflecting a state of "silent sensitization." This study illustrated that conventional diagnostic techniques for food allergy have low sensitivity and specificity in the diagnosis of allergy to meats.

- In another report of 12 patients with suspected beef allergy, all 12 patients had positive immunoassays to beef and 7 of the 12 reacted to either a labial or open-food challenge [75]. Two of the patients with positive challenges ingested 75 grams of beef before symptoms appeared, despite each having an IgE response of at least class III.

- In a third study of 10 adults with a history of recurrent food allergy symptoms on exposure to milk and meat, skin prick testing (SPT) with standard extracts for beef, pork, chicken, and milk produced negative results in all patients [26]. Immunoassays to meats and milk were positive in 9 patients.

- Some published data indicate that wheal reactions are consistently larger with fresh meat, suggesting the usefulness of the native allergen in meat allergy skin testing [18,77].

In summary, the utility of IgE determinations, either by skin testing or immunoassay, is less certain for the diagnosis of meat allergy than for many other food allergies.

Testing options — The following forms of testing **may** be required to demonstrate meat-specific IgE:

- Epicutaneous SPT with commercial extracts of meat.
- Epicutaneous skin testing with fresh meats (also called "prick-by-prick testing"). Details of the patient's history should guide preparation of the meat for testing. The meat should be cooked in a manner similar to the way the meat was prepared when it allegedly caused symptoms. As an example, if rare steak seemed to cause the reaction, then raw beef should be purchased and cooked rare just prior to the testing. We advise the patient to have a family member or friend cook the meat, to avoid having the patient handle raw meat to which he/she could be allergic.
- IgE immunoassays to individual meats.
- IgE immunoassays to galactose-alpha-1,3-galactose (alpha-gal), which are commercially available [78,79].
- IgE immunoassays to cat serum albumin, which are commercially available [80].
- Food challenge, or if feasible, DBPCFC. The total amount ingested during a challenge should mimic the amount ingested by the patient prior to developing symptoms. One study found that 75 grams of beef was necessary to identify allergy in some patients [75].

Diagnostic approach — Because of the issues discussed above, the best approach to diagnosis of meat allergy is not known. The author's approach is described here:

- In a patient who reports the relatively immediate onset of allergic symptoms following ingestion of meat, the author performs SPT to the meat(s) in question using commercial extracts initially. A different meat that the patient tolerates should be included as a negative control. If the SPT results are consistent with the patient's clinical history, a diagnosis of meat allergy is made for the specific meat(s). In the author's experience, commercial extracts produce small wheals (eg, usually, ≤4 mm in diameter) in sensitized patients [18].

  If SPT using commercial extracts is negative, SPT using fresh meat (so-called prick-by-prick testing) is then performed, again including a meat that is tolerated as a negative control. If this testing is positive to clinically suspected meat(s), then the diagnosis of meat allergy is confirmed.

  If prick-by-prick testing with fresh meats is negative, immunoassays are sent for the clinically suspected meats and a tolerated meat.

  In patients with suspected pork reactions who have not had reactions to beef or lamb, the author also tests for sensitization to cat, either with cat extract or with an immunoassay to cat serum albumin [80], to identify those patients with pork-cat syndrome. These patients usually report symptoms that begin within two hours of eating pork products, rather than the delayed reactions seen in patients sensitized to alpha-gal. (See 'Meats and animal dander/epithelium' above.)

  If all testing is negative, then food challenge is indicated if the patient wishes to pursue a more certain diagnosis. When feasible, this should be performed in a single- or double-blinded manner. (See "Oral food challenges for diagnosis and management of food allergies".)

- For patients who report symptoms that occur three to six hours after eating mammalian meat (or consistently occur at night, even if the association with meat ingestion is not clear), SPT are performed to commercial extracts of beef, pork, lamb, chicken, turkey, milk, and cat and dog dander.

  The author includes poultry in the testing to determine if the patient is sensitized to mammalian meats only or to an allergen found on nonmammalian meats also.

  Dog and cat are included for this reason too and to detect possible pork-cat syndrome. (See 'Meats and animal dander/epithelium' above.)

  Milk is included because it contains alpha-gal, and many patients with IgE to alpha-gal report difficulty tolerating milk.

  A meat that the patient tolerates is included as a negative control.

It has been the author's experience that skin testing with commercial extracts is often negative in patients who have IgE to alpha-gal.

If SPT using commercial extracts is negative, then prick-by-prick testing with fresh meat is performed next, again including a meat that is tolerated as a negative control. If this testing is positive to clinically suspected meat(s), then the diagnosis of meat allergy is confirmed.

If testing with fresh meats is not feasible or the results are negative, then immunoassays to detect IgE to alpha-gal may be performed. Immunoassays are commercially available [78,79].

If all testing is negative, then food challenge is indicated if the patient wishes to pursue a more certain diagnosis and there is a setting available in which challenges can be safely performed. When feasible, this should be performed in a single- or double-blinded manner. In the author's center, challenges to patients with negative tests as a single "dose" followed by three to six hours of observation have been administered. Food challenges are discussed in more detail separately. (See "Oral food challenges for diagnosis and management of food allergies".)

Diagnosis of non-IgE-mediated forms of allergy — The evaluation of patients with eosinophilic esophagitis (EE) or food protein-induced enterocolitis syndrome (FPIES) who are suspected to have sensitivity to foods is discussed elsewhere. (See "Food protein-induced enterocolitis syndrome (FPIES)", section on 'Diagnosis' and "Future diagnostic tools for food allergy", section on 'Gastrointestinal food allergy'.)

DIFFERENTIAL DIAGNOSIS

The following disorders can mimic meat allergy:

- Chronic spontaneous urticaria, especially when it first develops, can mimic an allergic reaction, especially if there is accompanying angioedema. Patients often question the foods most recently ingested. However, the persistence of chronic urticaria eventually distinguishes it from an allergic reaction.
- Severe irritable bowel symptoms can mimic the gastrointestinal symptoms of an allergic reaction, but symptoms outside of the gastrointestinal tract (eg, pruritus, urticaria, or angioedema, wheezing) would be absent. Still, in patients presenting with repeated episodes of abdominal cramping several hours after consuming mammalian meat, galactose-alpha-1,3-galactose (alpha-gal) allergy should be considered.
- Pork-cat syndrome is a type of meat allergy caused by sensitization to cat serum albumin, a protein, rather than the carbohydrate alpha-gal. Patients react to pork and variably to beef. Reactions tend to occur quickly after pork ingestion, distinguishing this disorder from the delayed reactions caused by alpha-gal. (See 'Pork/cat allergy' above.)
- Allergic reactions to antibiotics in meat, particularly penicillin and possibly streptomycin, can mimic meat allergy [81-83]. Patients allergic to penicillin will generally be aware of this, and penicillin skin testing can confirm the allergy. In contrast, allergy to streptomycin is rare and may not be apparent from the clinical history. Skin testing can be performed but has been associated with anaphylaxis and should be undertaken with caution [84].
- Adverse reactions to additives, such as natural colorings (carmine red or annatto), can also mimic food allergies. Allergic and asthmatic reactions to food additives are reviewed separately. (See "Allergic and asthmatic reactions to food additives".)

MANAGEMENT

Management of food allergy most commonly involves avoidance of the culprit meat(s). If the patient reacted to raw or rare meat, then it may be helpful to determine if the meat is tolerated in a well-cooked form, as the patient may be able to keep the food in his/her diet in cooked forms. Patients with immunoglobulin E (IgE)-mediated meat allergy should be equipped with an epinephrine autoinjector and taught how and when to use it. General issues in food-induced anaphylaxis and food allergen avoidance are reviewed elsewhere. (See "Food-induced anaphylaxis" and "Management of food allergy: Avoidance".)

A small number of reports of successful desensitization protocols have been published in both adults and children with alpha-gal allergy [85,86]. Since alpha-gal allergy appears to resolve over time without additional tick bites, it is unclear whether risks associated with immunologic desensitization offer benefit beyond the natural history of the syndrome [87].

NATURAL HISTORY

Children with cow's milk allergy who are also allergic to beef (representing the largest group of meat-allergic children) tend to outgrow both the beef and cow's milk sensitivities [88]. In one study, tolerance of beef was reached after a median duration of three years and has been reported to occur prior to tolerance to cow's milk in those allergic to both foods [88].

There is a paucity of published data regarding the natural history of meat allergy in adults. Case reports suggest that some individuals who acquired the allergy as adults lose the sensitivity over time [89]. One case report described a middle-aged patient with immunoglobulin E (IgE)-mediated allergy to several mammalian meats, who subsequently developed an allergy to bovine serum albumin (BSA). Three years later, he began to tolerate ingestion of cooked lamb and pork [90]. A review of 12 cases of beef allergy also reported that some patients became tolerant [75].

The natural history of reactions caused by sensitization to galactose-alpha-1,3-galactose (alpha-gal) is not well-studied. While there are no data from long-term series or controlled studies, initial evidence from the author's work suggests that IgE antibodies to alpha-gal decrease in some patients over time. However, additional tick bites appear to increase the antibody level (figure 1).

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Food allergy".)

SUMMARY AND RECOMMENDATIONS

- Meat allergy is uncommon. Exceptions are noted among certain patient groups: Children with atopic dermatitis and patients with delayed anaphylaxis in the southeastern United States. The prevalence of allergies to specific meats appears to be related to the prominence of a given meat in the diet. Allergy to beef is reported most commonly. (See 'Epidemiology' above.)
- Both immunoglobulin E (IgE)-mediated and non-IgE-mediated forms of meat allergy have been described. IgE-mediated reactions may be immediate or delayed up to three to six hours after ingestion. Non-IgE-mediated disorders in which meats have been implicated include eosinophilic esophagitis (EE) and pediatric food protein-induced enterocolitis syndrome (FPIES). (See 'Clinical reactions' above.)
- The main allergens in meats are serum albumins and immunoglobulins, both of which are significantly altered by cooking. This may partly explain why meat allergy is uncommon. A carbohydrate allergen has also been identified, galactose-alpha-1,3-galactose (alpha-gal), which seems to be particularly prevalent in patients in the southeastern United States. (See 'Allergens' above.)
- The similarity of various serum albumins leads to cross-sensitization among meats and/or allergy to milk and animal dander. Sensitization to alpha-gal can cause cross-sensitization to gelatins and the monoclonal antibody cetuximab. (See 'Patterns of cross-reactivity' above.)
- The diagnosis of meat allergy involves history, objective testing, and possibly food challenge. However, the sensitivity and specificity of tests for meat-specific IgE are relatively poor. The use of fresh meat for skin testing may improve sensitivity. (See 'Diagnosis' above.)
- Management largely consists of avoidance of the causative meat and patient education about how to self-inject epinephrine if needed for accidental exposures. (See "Food-induced anaphylaxis" and "Management of food allergy: Avoidance".)

- Many children and some adults become tolerant to meat over time. (See 'Management' above and 'Natural history' above.)

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Topic 2393 Version 22.0

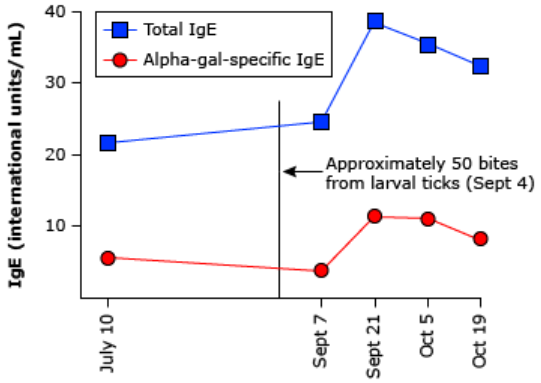
GRAPHICS

An adult female *Amblyomma americanum* (lone star tick)

Champman AS, Bakken JS, Folk SM, et al. Diagnosis and management of tickborne rickettsial diseases: Rocky Mountain Spotted Fever, Ehrlichoioses, and Anaplasmosis-United States: A practical guide for physicians and other health-care and public health professionals. MMWR Recomm Rep 2006; 55(RR-4):1.

Graphic 71086 Version 4.0

IgE to alpha-gal and total IgE following tick bites



The figure shows how levels of total IgE and alpha-gal-specific IgE both increased in the serum of a single patient following multiple tick bites.

IgE: immunoglobulin E.

Unpublished work from: Scott Commins, MD, Charles Lane, MD, and Thomas Platts-Mills, MD, PhD.

Graphic 89236 Version 3.0

Contributor Disclosures

Scott P Commins, MD, PhD Grant/Research/Clinical Trial Support: NIH/NIAID [Food allergy]. Speaker's Bureau: Genentech [Asthma, urticaria]. **Scott H Sicherer, MD, FAAAAI** Grant/Research/Clinical Trial Support: HAL Allergy [Food allergy]; Food Allergy Research and Education [Food allergy]; NIAID [Food allergy clinical trials]. Other Financial Interest: Johns Hopkins University Press [Royalties]. **Anna M Feldweg, MD** Nothing to disclose

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

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