# Idiopathic Anaphylaxis

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**KEYWORDS**

• Anaphylaxis • Idiopathic anaphylaxis • Mast cell activation syndrome

**KEY POINTS**

- Idiopathic anaphylaxis (IA) is a diagnosis of exclusion after other causes, such as foods, medications, exercise, insect stings, C1 esterase inhibitor deficiency, and mastocytosis, have been excluded.
- A significant proportion (24%–59%) of anaphylaxis cases are classified as idiopathic in several reported patient series. There is a higher prevalence of idiopathic anaphylaxis in women compared with men and a high prevalence of atopy in patients with IA.
- Classification of IA is based on frequency of episodes and clinical manifestations; frequent episodes are defined as at least 2 episodes in the preceding 2 months or at least 6 episodes in the preceding year.
- Treatment of IA is individualized based on severity and frequency of symptoms.
- Acute treatment of IA is the same as treatment of anaphylaxis from other causes, except that prolonged tapering of prednisone is usually required to induce remission. All patients should possess an epinephrine autoinjector and an anaphylaxis emergency plan.
- The prognosis of IA is generally favorable with appropriate treatment and patient education.

## BACKGROUND AND DEFINITION

The term idiopathic anaphylaxis (IA) refers to anaphylaxis without a discernible cause after completion of an appropriate diagnostic evaluation. It is a diagnosis of exclusion after other causes, such as foods, medications, exercise, insect stings, C1 esterase inhibitor deficiency, and mastocytosis, have been thoroughly considered and excluded. In 1978, Bacal and colleagues[1] reported the first cases of IA. In that report, of the 21 patients in the series, 11 had no causal explanation for anaphylaxis and the term IA was given. Initially, the medical community received the term IA with considerable doubt and skepticism because it was thought that an external cause or factors should

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be found for each case of anaphylaxis.[2] In addition, reports of IA were initially limited to the United States. However, in the 1990s, reports emerged from European countries, such as Spain, France, Ireland, Germany, and Brazil.[3] Subsequently, IA has become widely accepted as a disease process worthy of closer attention.

The pathophysiology of IA has not been fully elucidated, although elevated concentrations of urinary histamine and its metabolite, methylimidazole acetic acid, plasma histamine, and serum tryptase found in patients with this disorder is consistent with mast cell activation.[4] Manifestations of IA are identical to those episodes with a known cause. Despite early use of epinephrine autoinjector, some patients continue to experience life-threatening events, and there have been fatalities. There is a high prevalence of atopy in patients with IA with the rate found to be as high as 59% in one case series.[5] There is also a significantly higher prevalence in women compared with men.[6] However, after puberty and until menarche, the incidence has been reported to be similar in men and women.[6]

## CLASSIFICATION

The classification of IA is based on frequency of episodes and clinical manifestations.[7] Frequent episodes are defined as having at least 2 episodes in the preceding 2 months or at least 6 episodes in the preceding year. Patients who do not meet either of these 2 criteria are categorized as having infrequent IA (**Table 1**). Generalized IA (IA-G) is characterized by urticaria and/or angioedema in addition to systemic symptoms, including cardiovascular, respiratory, and/or gastrointestinal symptoms. Some patients are categorized as IA-angioedema (IA-A), which is characterized by significant upper airway obstruction due to severe angioedema of the tongue, pharynx, or larynx without other signs of systemic anaphylaxis; patients may also have urticaria.

**Table 1**
**Classification of idiopathic anaphylaxis**

| Parameter | | Comments |
|---|---|---|
| Classification | IA-G | Urticaria or angioedema with bronchospasm, hypotension, syncope |
| | IA-A | Angioedema with upper airway compromise (laryngeal, pharyngeal, tongue); may also have urticaria |
| Frequency | Frequent (F) | Definition: At least 2 episodes in the preceding 2 mo or at least 6 episodes in the preceding year |
| | Infrequent (I) | Definition: Fewer than 6 episodes a year |
| Severity | CSD-IA | Patient cannot be tapered off prednisone |
| | MCSD-IA | Patient requires at least 20 mg every day or 60 mg every other day prednisone to control IA |
| Variations of IA | IA-Q | Patient has possible IA but documentation of objective findings are unsuccessful and diagnosis is uncertain |
| | IA-V | Applied when symptoms of IA vary from classic IA |
| | Somatoform IA (IA-S) | Symptoms mimic IA but patients have no organic disease, documented objective findings, and are nonresponsive to the treatment regimen for IA |

*Adapted from* Patterson R. Idiopathic anaphylaxis. East Providence (RI): OceanSide Publications, Inc; 1997. p. 20.