

# Symptoms and manifestations of anaphylaxis recur in a stereotypic sequence in individuals

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## Abstract

**Background:** This study was undertaken to address whether recurrent anaphylaxis to specific allergens in individuals follows a stereotypic sequence of symptoms.

**Methods:** Data were extracted from charts of patients seen between 2012-2018 at a tertiary care allergy clinic. The sequence of appearance of symptoms of anaphylaxis was recorded at each patient visit and used for analysis. Only patients who had anaphylaxis to single allergens were included. A total of 3,174 anaphylactic reactions in 162 patients were analyzed by Fleiss' Kappa method to assess for reproducibility of the order of appearance of specific symptoms during anaphylaxis in individual patients.

**Results:** The mean age at first visit was 36.0 years (SD = 14.2; range 1-71 ). Seventy-seven percent (124/162) of patients were female. The mean kappa was 0.93, 5<sup>th</sup> percentile was 0.5 and the 95<sup>th</sup> percentile was 1.0. Seventy-nine percent of participants had a Fleiss' kappa of 1.0, indicating that 86% of people had an identical sequence of symptoms with every one of their anaphylactic reactions. However, the sequence of symptoms differed markedly between patients, even for the same allergen.

**Discussion:** These data suggest that the large majority of people with recurrent anaphylaxis will have the exact same sequence of symptoms with subsequent reactions. Teaching individuals to recognize patient-specific sequence of symptoms will allow them to earlier identify anaphylaxis with the opportunity to administer therapeutic interventions earlier.

## Background

This study was undertaken to address whether recurrent anaphylaxis to specific allergens in individuals follows a stereotypic sequence of symptoms.

## Methods

We conducted a retrospective chart review of patients seen in a tertiary care allergy clinic at a university teaching hospital from 2012-2018. This study was approved by the research ethics board of St. Michael's Hospital.

Electronic records were searched using key words including "stereotypic" and "anaphylaxis". The course of these patients' anaphylactic reactions, including order of symptoms and interventions, were recorded. All anaphylactic triggers were recorded including: foods, medications, mast cell disorders and Hymenoptera insect stings.

The Brown Anaphylaxis score was used to capture severity of anaphylaxis. Scores of 1 indicate skin or subcutaneous tissue involvement only; scores of 2 being GI, cardiovascular and/or respiratory involvement; and scores of 3 being hypoxia, hypotension or neurologic compromise.<sup>1</sup>

Only patients who had anaphylaxis to single allergens were included. A total of 3,174 anaphylactic reactions in 162 patients were analyzed by Fleiss' Kappa method to assess for reproducibility of the order of appearance of specific symptoms during anaphylaxis in individual patients. This method of agreement was used to quantify the agreement of the order of the symptoms.

1. Brown SG. *Clinical features and severity grading of anaphylaxis*. J Allergy Clin Immunol. 2004;114(2):371-6.

## Results

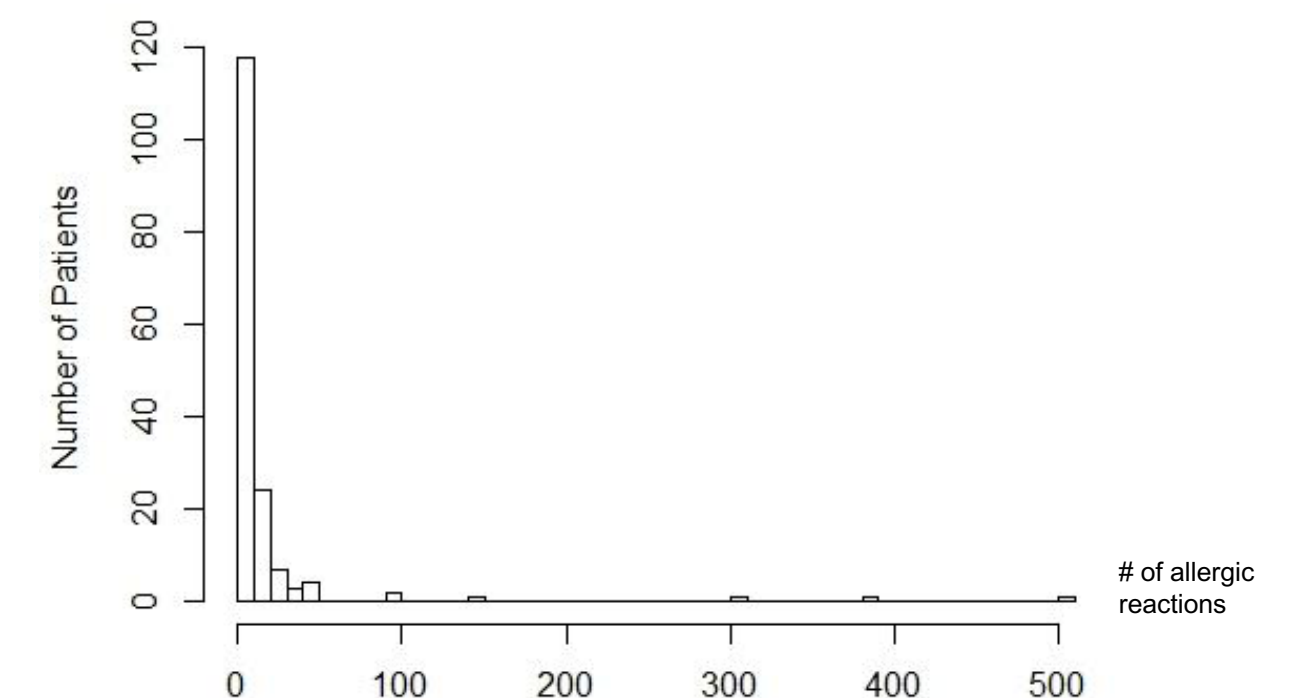
	Overall
n	162
Sex = Female (%)	124 (76.5)
Age at time of first visit (mean (SD))	35.98 (14.20)
Number of allergic reactions per patient (median [IQR])	6.00 [3.00, 15.00]
Allergy Severity score – patient level (%)	
1	2 ( 1.2)
2	124 (76.5)
3	36 (22.2)

Table 2: Allergies in the dataset

Allergen	n	%
Food	987	31.1
Mast cell disorder	726	22.9
Unknown	639	20.1
Cholinergic	494	15.6
Catamenial	120	3.8
Food-dependent exercise-induced	79	2.5
Exercise	47	1.5
Drug	34	1.1
Other triggers	48	1.5

Fleiss' kappa statistic ranged from -0.33 to 1.0, 159 out of 162 values (98.1%) of values were greater than 0.26 and 79% of all Kappa values were 1.0. There were 866 out of 3174 (27.3%) episodes where epinephrine was administered

Figure 1: Distribution of reactions



## Discussion

This is the first study to investigate whether any given patient's anaphylactic reactions progress through the same pattern of symptoms across multiple exposures.

Our analysis confirmed our hypothesis that reactions would be stereotypic in any given patient, for the overwhelming majority of patients.

Given our large sample size (n=162; 3174 reactions) across a wide range of ages with varying allergies, we believe our findings to be generalizable to all anaphylactic patients.

Even when reactions were spaced apart, sequence of symptoms and recruitment of different organ systems does not appear to change.

Knowing one's sequence of symptoms allows for earlier identification of anaphylaxis, with the opportunity to administer therapeutic interventions earlier. Furthermore, a patient's deviation from his/her normal sequence of symptoms during anaphylaxis may imply the existence of additional allergies.

## Conclusions:

This is the first study to demonstrate that anaphylactic reactions may manifest stereotypically in any given patient. This underscores a need to understand which organ systems are stereotypically involved in a particular patient's anaphylactic response, and also, the sequence of symptoms.