Is there anything that increases the risk of biphasic anaphylactic reactions?

Lee JM and Greenes DS. Biphasic anaphylactic reactions in pediatrics. Pediatrics 2000;106:762-766.

Take Home Message: The rate of biphasic anaphylactic reactions was 6%, and delayed administration of epinephrine was associated with an increased incidence of having a biphasic reaction.

Highlights: Biphasic anaphylactic reactions – the recurrence of anaphylactic symptoms after an initial remission – have been described in both children and adults. Prior to this study, there were no studies measuring the rate of or risk factors for biphasic anaphylactic reactions in children. Published in 2000, this retrospective study[i] analyzed 108 cases of anaphylaxis admitted to Boston Children's Hospital over 14 years. The rate of biphasic reactions was found to be 6%. Delayed administration of subcutaneous epinephrine was the only factor found to be associated with an increased risk of biphasic reaction, with a median time to epinephrine of 190 minutes in those who had a biphasic reaction vs. 48 minutes in those who did not (P=0.03). This association was also noted in a previous landmark case series by Sampson et al.[ii] Interestingly, in Lee and Greene's study, the asymptomatic intervals between initial anaphylaxis and biphasic reaction varied from 1.3 hours to 28.4 hours, so the authors conclude that only 2% of the patients benefitted from a 24-hour observation policy. This study further demonstrates the importance of administering epinephrine as early as possible to those having an anaphylactic reaction.

The Nitty-Gritty:

- **Design:**

- Retrospective analysis
- N= 108
- Setting: Boston Children's Hospital
- Enrollment: 1985-1999
- Primary outcome: Biphasic reaction

- **Population:**
  - **Inclusion Criteria:** children admitted with acute anaphylaxis (acute allergic reaction with involvement of at least 2 body systems: dermatologic, neurologic, gastrointestinal, respiratory, or cardiovascular)
  - **Exclusion Criteria**
    - Anaphylaxis developed during hospitalization for another reason
    - Patient had diagnosis of chronic idiopathic anaphylaxis
  - **Baseline Characteristics**
    - Male: 61.1%
    - Age
      - <1 year: 3.7%

- 1-5 years 29.6%
- 6-11 years: 35.2%
- 12-21 years: 31.5%

§ Trigger

- Food: 47.2% (27% tree nuts, 24% peanuts, 16% seafood)
- Medications: 22.2%
- Insect bites: 11.1%
- Immunotherapy 2.8%
- Immunizations: 0.9%
- Contrast dye: 0.9%
- Unknown: 14.8%

§ Route of Exposure

- Oral: 60.2%
- Subcutaneous: 16.7%
- Intravenous: 7.4%

- Inhaled: 1.9%

- Unknown 13.9%

§ Setting of Anaphylactic Event

- Home: 15.7%

- Doctor's office: 5.6%

Outdoors: 5.6%

- Emergency department: 5.6%

- Not documented: 61.1%

- **Intervention**:

o Data regarding past medical history, circumstances of allergen exposure, prehospital therapy, presenting signs and symptoms, treatment and hospital course were collected retrospectively from the medical records of children admitted with anaphylaxis

o The rates of serious symptoms, resolution of anaphylaxis, biphasic reaction and significant biphasic reactions (requiring oxygen, vasopressors, intubation, subcutaneous epinephrine or unscheduled bronchodilators) were calculated

- **Outcomes:** Based on 105 children with resolution of anaphylaxis (2 patients had fatal anaphylaxis and 1 had a protracted reaction)

o Incidence of a biphasic reaction: 6% (3% with a significant biphasic reaction)

- § All involved the same body systems affected initially
- § Asymptomatic intervals ranged from 1.3 hours to 28.4 hours

o Risk factors for biphasic reactions – comparisons are biphasic reaction vs. no biphasic reaction

- § Male: 50% vs. 63.6% (NS)
- § Mean age: 8.0 years vs. 8.6 years (NS)
- § Trigger ingested orally: 66.7% vs. 59.6% (NS)
- § Epinephrine given initially: 100% vs. 90.9% (NS)
- § Median time to initial dose of epinephrine: 190 minutes vs. 48 minutes (P=0.03)
- § Steroids given initially: 83.3% vs. 84.8% (NS)

[i] Lee JM and Greenes DS. Biphasic anaphylactic reactions in pediatrics. Pediatrics 2000;106:762-766.

[ii] Sampson HA, Mendelson L, Rosen JP. Fatal and near-fatal anaphylactic reactions to food in children and adolescents. N Engl J Med 1992; 327: 380-384.