A Framework For Anaphylaxis

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PGY4

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Outline

- Defining Anaphylaxis
- Incidence and Prevalence
- Triggers of Anaphylaxis
- Pathophysiology of Anaphylaxis
- Clinical Manifestations
- Clinical Course
- Clinical Approaches
- Management and Prevention
- Conclusions

"It's not you—it's my anaphylaxis."

General Descriptive Definition: Anaphylaxis

- "Anaphylaxis is an acute, allergic systemic reaction, during which all or some of the following are present: urticaria/angioedema, upper airway obstruction, bronchospasm, and hypotension. In some cases, these manifestations may be accompanied by cardiovascular and/or gastrointestinal disturbances. Anaphylaxis can be fatal without evidence of cutaneous involvement."

Adapted from Joint Task Force on Practice Parameters, American Academy of Allergy, Asthma and Immunology, American College of Allergy, Asthma and Immunology, and the Joint Council of Allergy, Asthma and Immunology. 1998.

World Allergy Organization Nomenclature

Classic Terminology

- Anaphylaxis
- Anaphylactoid

New Terminology

- Anaphylaxis
  Immunologic
  - IgE
  - Non IgE
- Anaphylaxis
  Non-immunologic

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Epidemiology of Anaphylaxis

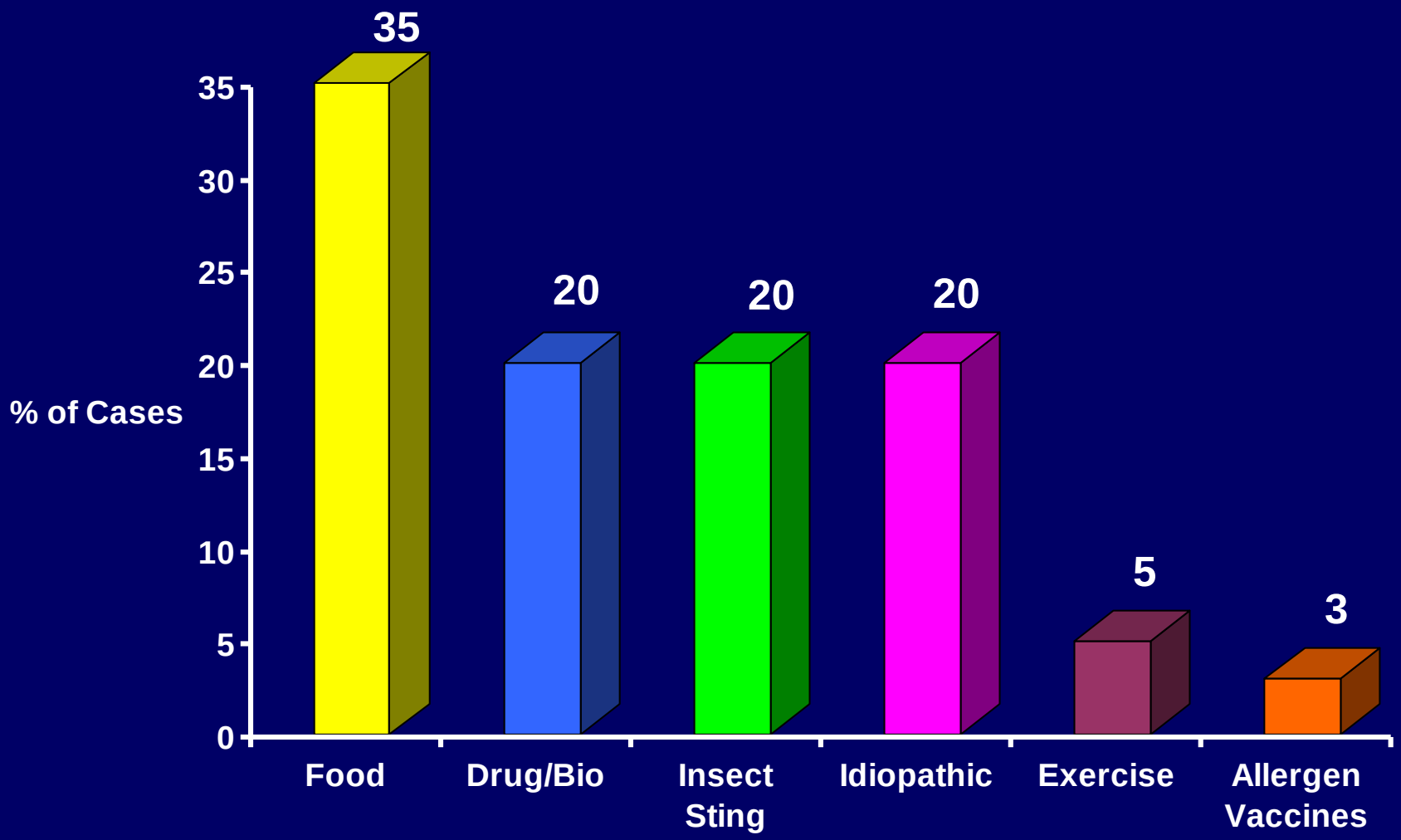
- 1-15% of US population (2.8 to 42.7 million people) may be at risk
- Estimated annual incidence
  - 21/100,000 (Yocum et al)
- Incidence of anaphylaxis is increasing

Factors Affecting the Incidence of Anaphylaxis

- Atopy
- Gender
  - In general, females > males
    - Unless < 15 years old, then M > F
  - For insect stings
    - male/female ratio is 3:2
- Age
- Route of administration (IV>PO)
- Economic status (resources available)
- Season

J Allergy Clin Immunol. 2001;105. Sheikh A, Alves B.*Clin Exp Allergy*. 2001; 31:1571-1576.

Overview of Anaphylactic Triggers



Golden. *Anaphylaxis*, 2004

Food-Induced Anaphylaxis: Common Triggers

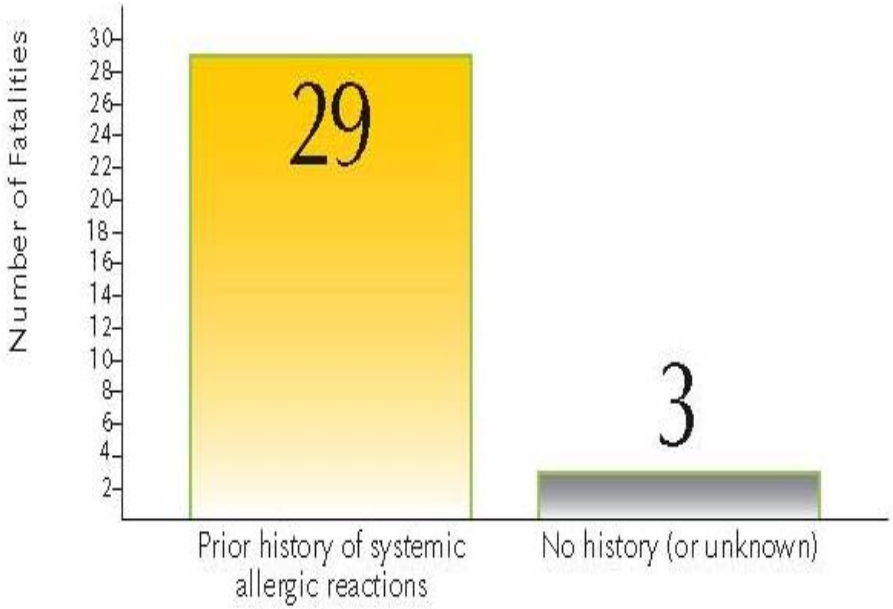
- Children and adults
  - Peanuts
  - Tree nuts
  - Shellfish
  - Fish
- Additional triggers in children (commonly outgrown)
  - Milk
  - Eggs
  - Soy
  - Wheat
- The above 8 foods account for 90% of all allergic reactions to food

The Food Allergy and Anaphylaxis Network (FAAN). Available at: http://www.foodallergy.org/anaphylaxis.html. Accessed January 28, 2005.

Fatal Food-Induced Anaphylaxis:

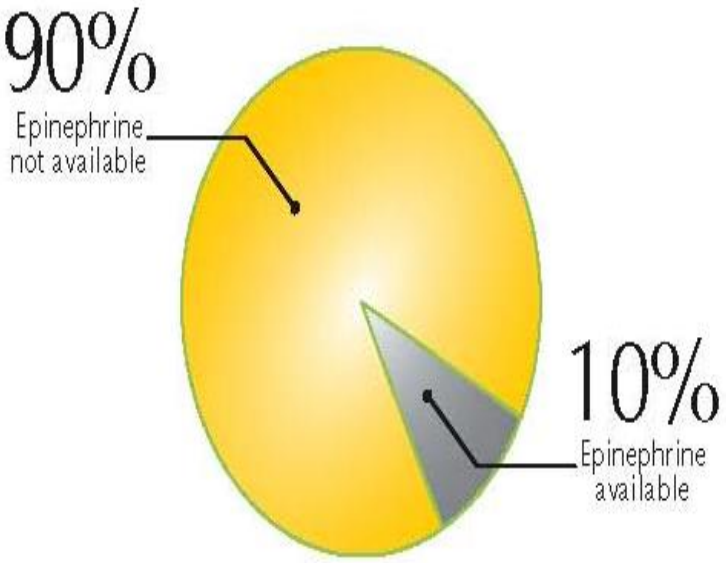
A clinical review of anaphylactic fatalities (N=32)

29 of 32 fatalities had a history of systemic allergic reactions



Adapted from Bock et al.

90% of the fatalities had no epinephrine available for use at the time of their reaction



Fatalities due to anaphylactic reactions to food

Adapted from Bock et al.

Bock SA, Muñoz-Furlong A, Sampson HA. Fatalities due to anaphylactic reactions to foods. *J Allergy Clin Immunol*. 2001;107:191-193.

Venom-Induced Anaphylaxis: Incidence

- 0.5% to 5% of Americans are sensitive to 1 or more insect venoms
  - Hymenoptera order of insects
    - Bees
    - Wasps
    - Yellow jackets
    - Hornets
    - Fire ants
- At least 40 to 100 deaths per year
- **Immunotherapy 98-99% effective to prevent reactions**

Neugut AI, Ghatak AT, Miller RL. *Arch Intern Med.* 2001;161:15-21.

Latex-Induced Anaphylaxis: Incidence

- Up to 6% of U.S. (16 million) affected
- Up to 17% among healthcare workers!
- Latex gloves
- Incidence has increased

Neugut AI, Ghatak AT, Miller RL. *Arch Intern Med.* 2001;161:15-21. The Food Allergy and Anaphylaxis Advocacy Network (FAAN). Available at: http://www.foodallergy.org. Accessed November 2, 2004.

Medication-Induced Anaphylaxis: Incidence

- ~ 550,000 serious allergic reactions to drugs/year in U.S.
  - Penicillin has highest number of deaths each year
  - Reactions more severe IV vs PO route
- Most common drugs:
  - Antibiotics - beta-lactams
  - Aspirin, NSAIDs

Neugut AI, Ghatak AT, Miller RL. *Arch Intern Med*. 2001;161:15-21., Lazarou J, Pomeranz BH, Corey PN. *JAMA*. 1998;279:1200-1205.

Triggers of Anaphylaxis: Physical

- Exercise-induced anaphylaxis
  - May be food dependent or independent
  - May be more common than previously realized
- Cold-induced
- Heat-induced

Idiopathic Anaphylaxis

- Triggers unknown in spite of skin testing, extensive dietary history, and assessment of all possible causes, such as mastocytosis
- 1 study, more than 70% of cases were found to be idiopathic

Medem-ACAAI Medical Library Web site. Available at: http://www.medem.com/medicallibrary/anaphylaxis/.medem-ACAAI. Accessed November 1, 2004., Brunell PA, Bellanti JA, Gawchik SM, et al. *Infect Dis Child.* (CME training materials.) April 2004.

Pathophysiology of Anaphylaxis

Pathogenesis of Anaphylaxis

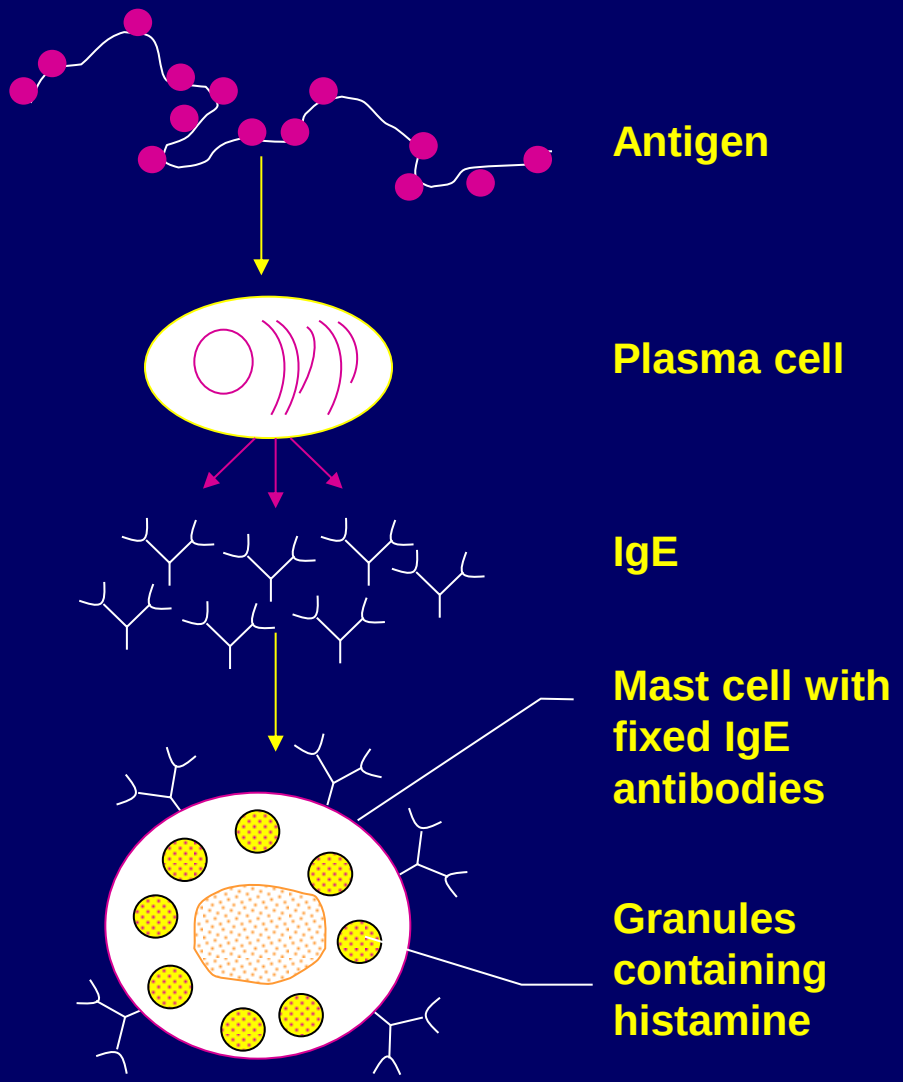
- IgE-mediated (Type I hypersensitivity)
- Sensitization stage
- Subsequent anaphylactic response

Sensitization Stage

① Antigen (allergen) exposure

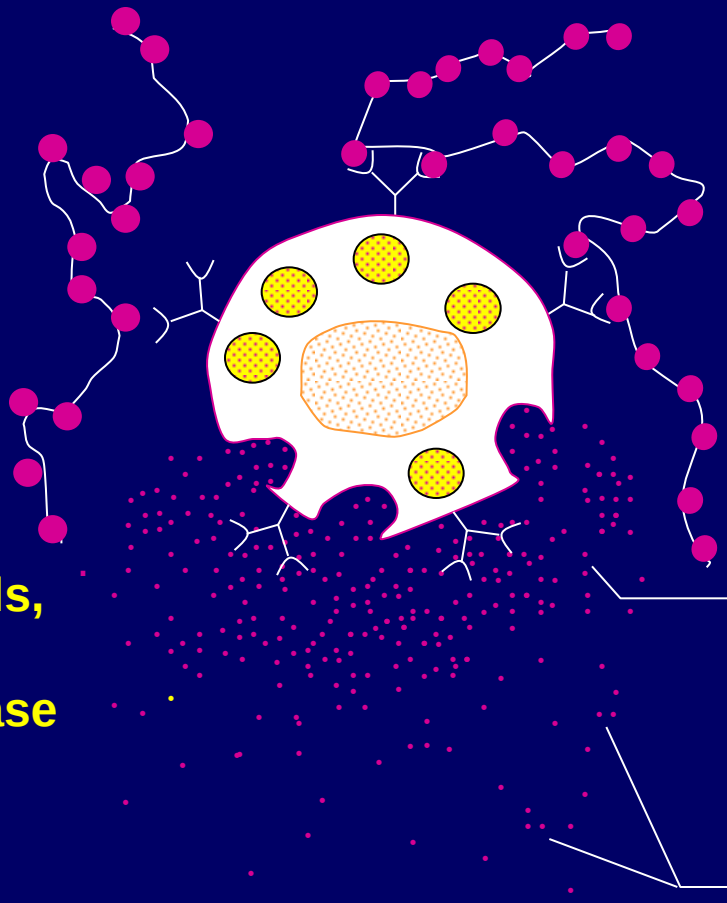
② Plasma cells produce IgE antibodies against the allergen

③ IgE antibodies attach to mast cells and basophils



Anaphylactic Reaction

④ More of same allergen invades body



⑤ Allergen combines with IgE attached to mast cells and basophils, which triggers degranulation and release of histamine and other chemical mediators

Most Frequent Signs and Symptoms of Anaphylaxis

Manifestation	Percent (%)
Urticaria angioedema	88
Upper airway edema	56
Dyspnea/wheeze	47
Flush	46
Hypotension	33
Gastrointestinal	30

Lieberman P. *Allergy Principles and Practice*. 2003.

Less Frequent Signs and Symptoms of Anaphylaxis

Manifestation	Percent (%)
Rhinitis	16
Headache	15
Substernal pain	6
Itch without rash	4.5
Seizure	1.5

Lieberman P. *Allergy Principles and Practice*. 2003.

Tryptase and Histamine

- Serum Tryptase
  - Peaks 60 to 90
  - Remains elevated as long as 5 hours
- Plasma histamine
  - Rises in 5 minutes
  - Remains elevated only 30 to 60 minutes
- Urinary histamine metabolites
  - Remains elevated as long as 24 hours
- Under ideal conditions, the PPV of a serum tryptase can be 92.6%, but the NPV is only 52%

Anesthesiology 99:536,2003

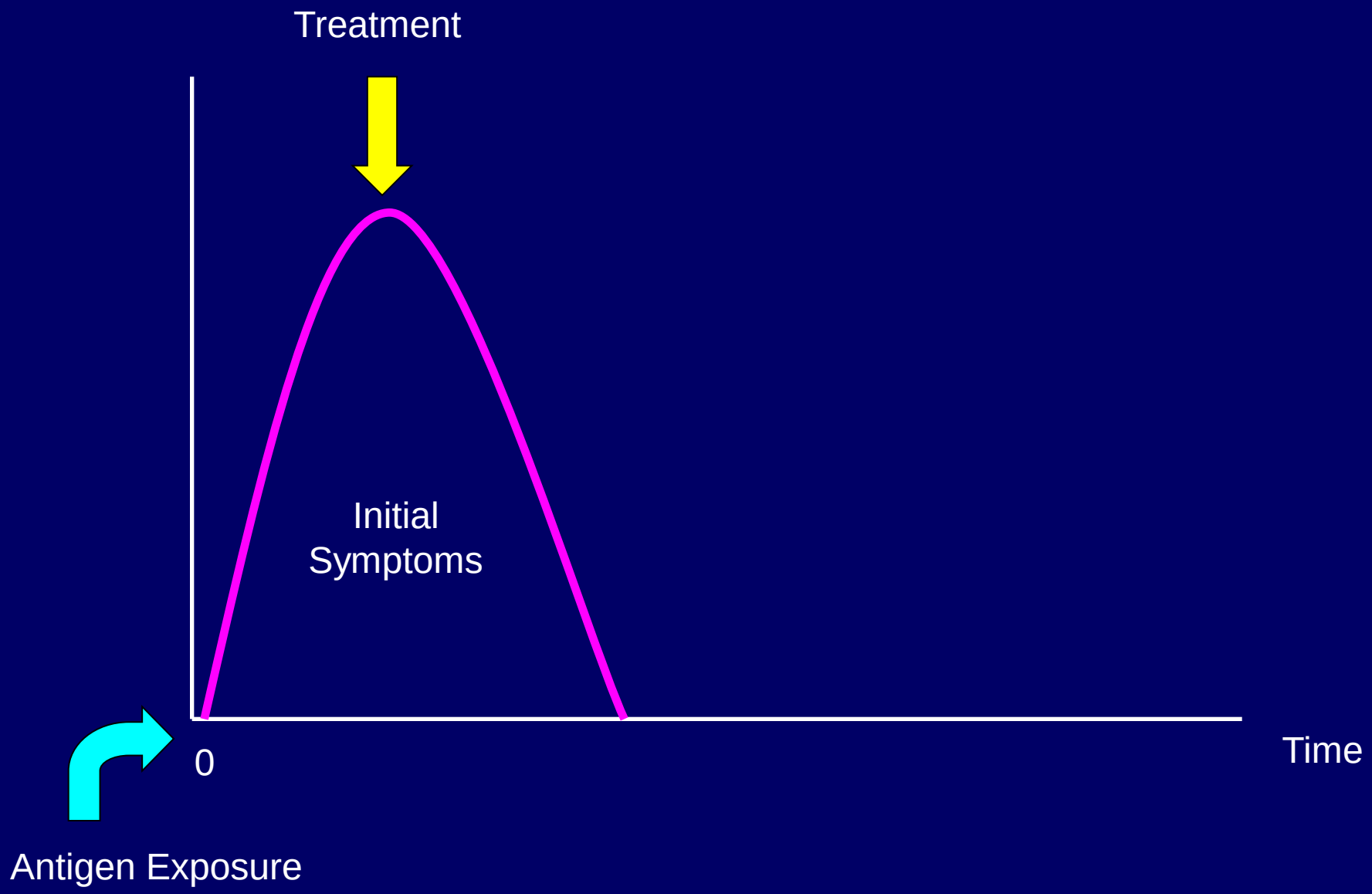
Clinical Course of Anaphylaxis

Patterns of Anaphylaxis

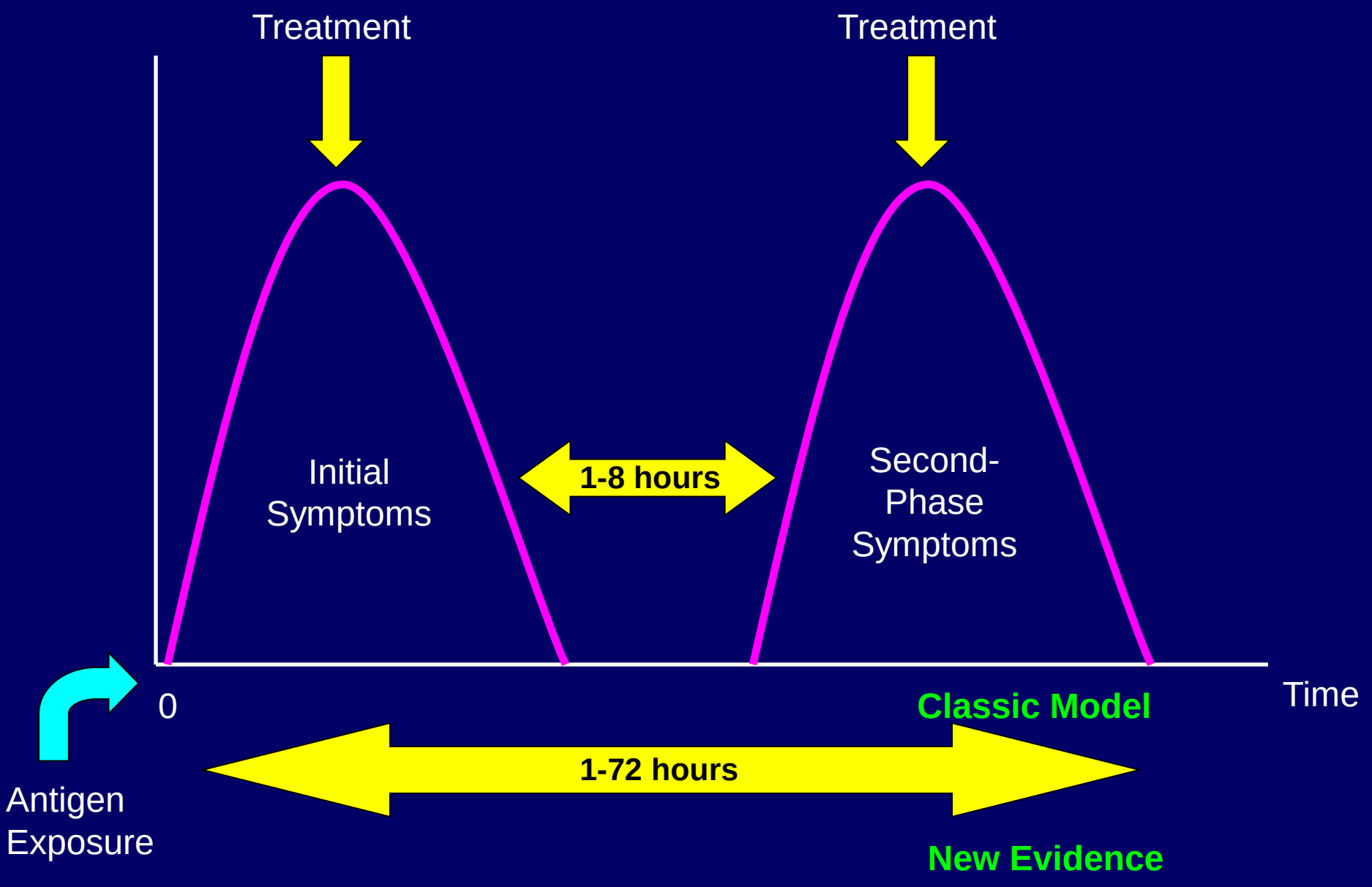
- Uniphasic
- Biphasic
- Protracted

Lieberman, 2004

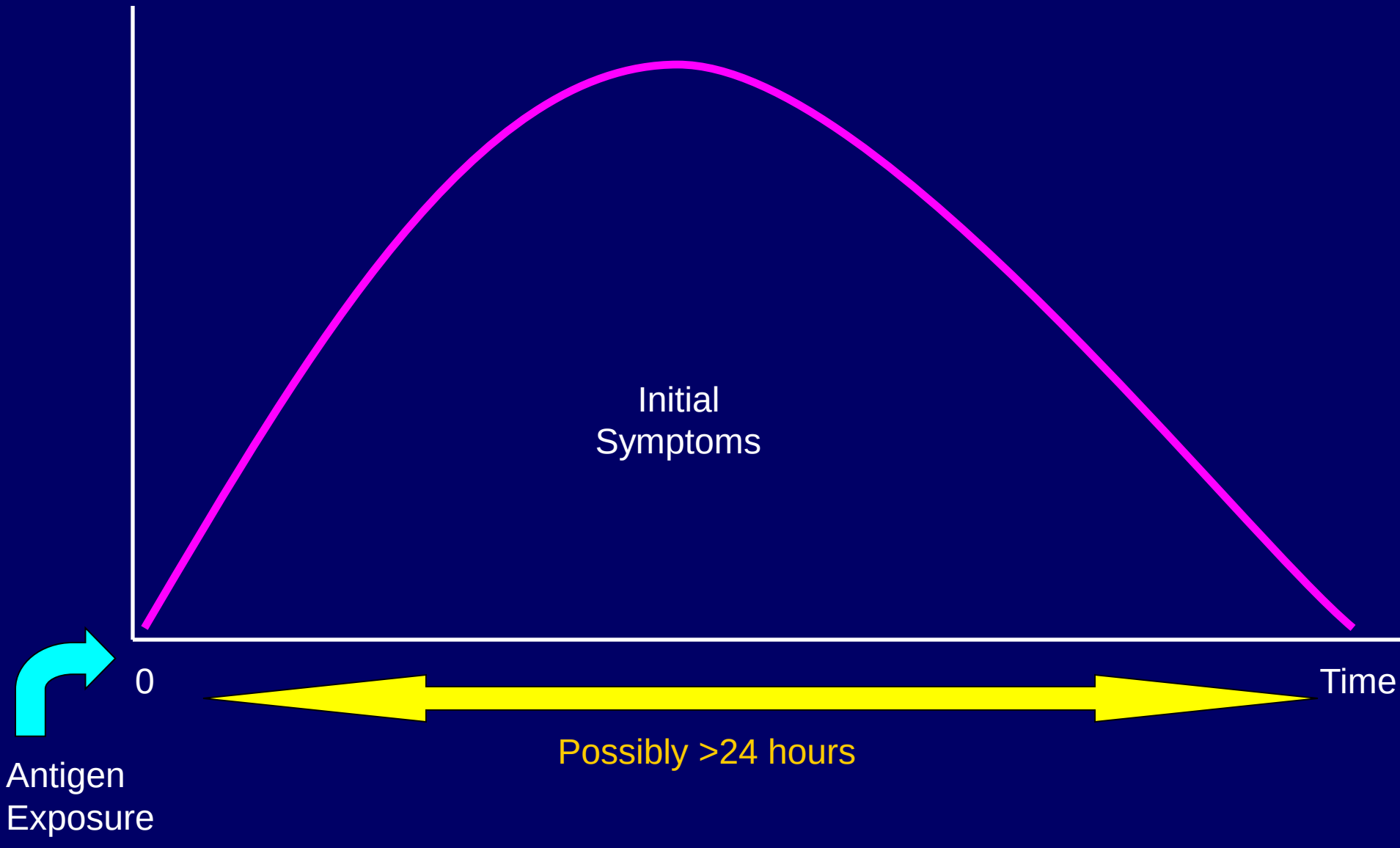
Uniphasic Anaphylaxis



Biphasic Anaphylaxis

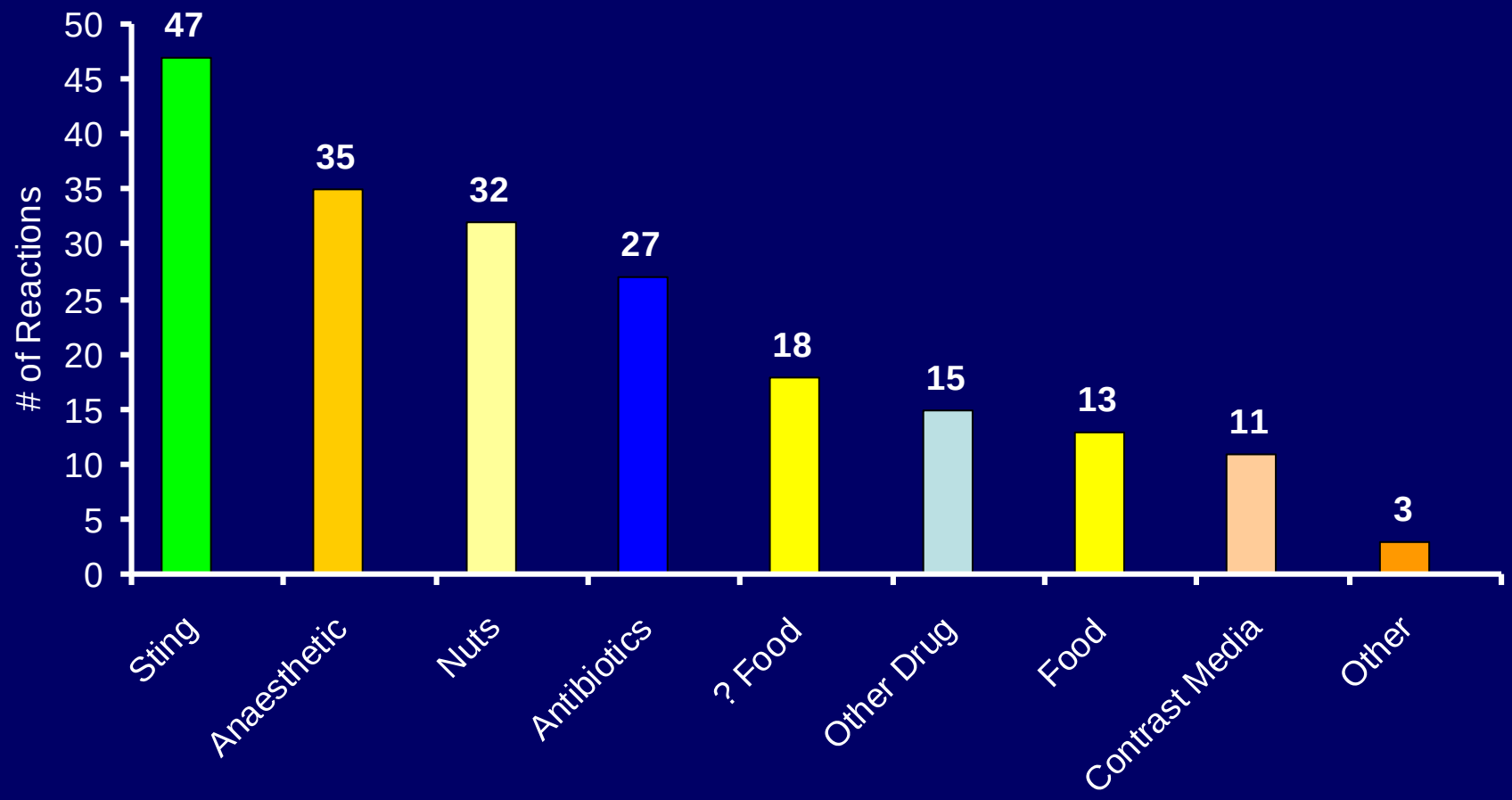


Protracted Anaphylaxis



Fatal Reactions

Etiology of Fatal Reactions



Pumphrey, 2004

Fatalities Associated With:

- Delay in time of onset to treatment
- History of asthma or cardiac disease
- Rapid IV allergen
- Beta blocker use
- However, most fatal reactions are unpredictable

Pumphrey, *Curr Opin Allergy Clin Immunol 2004;* Sampson et al, *N Engl J Med, 1992;* Pumphrey, *Clin Exp Allergy, 2000*

Myth: Prior Episodes Predict Future Reactions

REALITY:

- No predictable pattern
- Severity depends on:
  - Sensitivity of the individual
  - Dose of the allergen

Management & Prevention of Anaphylactic Episodes

Management of the Acute Event: Immediately

- Place in recumbent position, feet elevated
- Check airway and secure if necessary
- **Administer epinephrine**
- Initiate oxygen
- Early and aggressive treatment to maintain airway, blood pressure and cardiac output

Lieberman P. *Annals Allergy Asthma Immunol.* 2005;95:217.

Treatment of Anaphylaxis

- Corticosteroids
- Repeat epinephrine if Sx persist or increase after 10-15 minutes
- Supplemental O_2; airway maintenance
- IV fluids, vasopressor therapy
- Repeat antihistamine ± H_2 blocker if Sx persist
- Observe for a minimum 4 hours
- Arrange follow-up care, provide epinephrine Rx and education

Myth: Epinephrine is Dangerous

REALITY:

- Risks of anaphylaxis far outweigh risks of epinephrine administration
- Minimal cardiovascular effects in children
- Caution when administering epinephrine in elderly patients or those with known cardiac disease
- There is no absolute contraindication to epinephrine use in anaphylaxis

Epinephrine Is Underutilized for Acute Treatment

- Only 30% who required epinephrine actually received it
- Used in 62% of fatal reactions but only 14% of reactions received it **before** cardiac arrest
- Physicians often fail to diagnose anaphylaxis correctly
  - Can be confused with other conditions

Sampson et al, *N Engl J Med*, 1992.; Pumphrey, *Clin Exp Allergy*, 2000; Gold and Sainsbury, *J Allergy Clin Immunol*, 2000

Prevention of Anaphylactic Episodes and Fatalities

- Obtain a good history!
- Avoidance, avoidance, avoidance – most is common sense
- Patients must always be prepared
- Instruct patients to wear MedicAlert® bracelets
- Check all drugs for proper labeling

Lieberman P. *Allergy Principles and Practice.* 2003.

Venom-Induced Anaphylaxis: Avoidance Measures

- Seek professional help in removing hives or nests
- Keep outdoor areas free of garbage
- Avoid using scented products
- Avoid wearing bright colors outdoors during the day
- Wear closed shoes and not go barefoot outside
- Not drink from open cans when contents are not visible

Allergy Principles and Practice. Mosby Publications: Yunginger J. 2004.

Latex-Induced Anaphylaxis: Avoidance Measures

- Use latex-free products
- Alert employers, healthcare providers, school personnel about the need for latex-free products and equipment
- Be aware of possible cross-sensitivity to certain foods
  (eg, banana, avocado, kiwi, chestnut, etc)

American Academy of Allergy, Asthma and Immunology Web site. Available at: http://www.aaaai.org/patients/resources/fastfacts/latex.stm. Accessed November 5, 2004.

Patient Challenges

- Failure to carry epinephrine auto-injector
- Delayed treatment – often associated with fear of needles and/or medication
- Failure to administer second injection when needed
- Inadequate treatment and patient education
  - Failure to prescribe epinephrine auto-injector
  - Patients may misuse auto-injectors
  - Insufficient amount of epinephrine injected
  - Use of outdated epinephrine

Conclusions

Awareness Must Increase

- Anaphylaxis is a life-threatening acute reaction which is under-reported, frequently misdiagnosed, and under-treated
  - More common than previously thought
- Rapid and proper administration of epinephrine is the standard of treatment
  - Many patients require a second epinephrine injection to treat anaphylaxis

Final Thoughts

- Physician and patient awareness levels need to be increased to properly prevent, diagnose, and treat anaphylaxis

- Patient should be directed to the emergency room for follow-up care after the first dose of epinephrine for the treatment of anaphylaxis

Epinephrine Dosing

- IM injection in lateral thigh produces most rapid rise in blood level
  - 0.01mg/kg in children
  - 0.3-0.5mg in adults
- Data suggest that up to 35% of patients require more than a single epinephrine injection

Korenblat and Day, *Allergy Asthma Proc*, 1999; Montanaro and Bardana. *J Investig Allergol Clin Immunol*, 2002

Epinephrine: The Treatment of Choice for Anaphylaxis

- **Epinephrine is the treatment of choice for all anaphylactic episodes**

Sicherer S. *J Respir Dis Pediatrician*. 2003;5(5):191-198.
Simons FE. *J Allergy Clin Immunol.* 2004;113:837-844.

Thank you