Emergency Management of Acute Allergic Reactions and Anaphylaxis

Sunday Clark, MPH, ScD

April 12, 2007
Background & Significance

- Acute, systemic reaction caused by mast cell-mediator release that is potentially life threatening
- Anaphylaxis occurs when the body has responded to proteins introduced to the body (e.g., in food), by creating an antibody called immunoglobulin E (IgE)
- Identified by multi-system organ involvement reacting to mast cell degranulation and mediator release temporarily associated with a specific trigger
Background & Significance (continued)

- Lifetime prevalence of anaphylaxis in westernized countries has been difficult to determine
  - Population-based study estimated <1%
  - More recent estimates vary ranging from 0.3-0.6% to 0.95%

- Anaphylaxis due to specific causes
  - Food-related anaphylaxis estimates: 1.1 – 2.3%
  - Insect sting-related anaphylaxis estimates: 0.4 – 5%
Background & Significance (continued)

- Burden of anaphylaxis in emergency department (ED) also uncertain

- Food-related allergic reactions recently cited to be leading cause of allergic reactions treated in ED
  - Approximately 30,000 cases annually

- Estimates also suggest 2,000 hospitalizations and 150-200 deaths each year
Best method for identifying acute allergic reactions and anaphylaxis is unclear

- Treatment guidelines (AAAAI, 1998) recommend
  - Prescription for self-injectable epinephrine
  - Referral to an allergy specialist
  - Education: Allergen avoidance
ICD-9 Coding of Emergency Department Visits for Food and Insect Sting Allergy

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Ann Epidemiol 2006; 16: 696-700
Introduction

- The number of ED visits each year for food and insect sting-related allergy is uncertain.

- Although a statistical summary of discharge diagnoses would be of interest, it is unclear how ED visits for these allergies are actually coded.

- In 1997, the ICD-9 coding system introduced codes to identify specific food allergies.

- The extent to which existing and newer ICD-9 codes for allergic disorders are implemented is unknown.
Objectives

- To determine the accuracy of using ICD-9 codes to identify ED visits for food-related and insect sting-related allergic reactions

- To describe potential differences between patients who are coded with specific ICD-9 codes and those coded with more general codes
ICD-9 Codes

- **Food-related**
  - 693.1 (dermatitis due to food)
  - 995.60 (allergy due to unspecified food)
  - 995.61-995.69 (allergy due to specified foods)

- **Insect sting-related**
  - 989.5 (toxic effect of venom)

- **Non-specific codes**
  - 995.0 (other anaphylactic shock)
  - 995.3 (allergy, unspecified)
Identification by Allergy-Specific ICD-9 Codes

- Food allergy
- Insect sting allergy
Among 775 consecutive ED patients presenting with an acute allergic reaction, 216 (28%) were coded as having food allergy.

Of the remaining 559 patients with unspecified allergy, 190 (34%) were identified by chart review as having definite/probable food allergy.

Thus, only 53% (95% CI, 48-58%) of 406 patients with a food-related allergic reaction had an ICD-9 code indicating food allergy.
Food-Related Reactions (continued)

- ICD-9 code identified patients were less likely to be white and more likely to have documentation of a history of asthma.
- The ICD-9 identified group was more likely to have cutaneous and cardiovascular signs or symptoms.
- This group was less likely to have anaphylaxis and were more likely to be sent home.
Discharge Instructions

Avoid offending allergen
Prescribed self-injectable epinephrine
Referred to an allergist

<table>
<thead>
<tr>
<th>Avoid offending allergen</th>
<th>Prescribed self-injectable epinephrine</th>
<th>Referred to an allergist</th>
</tr>
</thead>
<tbody>
<tr>
<td>p=0.43</td>
<td>p=0.18</td>
<td>p=0.009</td>
</tr>
</tbody>
</table>

ICD-9 identified
Chart review identified

food
Insect Sting-Related Allergic Reactions

- Among 620 consecutive ED patients presenting with an acute allergic reaction, 341 (55%) were coded as having insect sting allergy.

- Of the remaining 279 patients with unspecified allergy, 53 (19%) were identified by chart review as having definite/probable insect sting allergy.

- Thus, 87% (95% CI, 83-90%) of 394 patients with a insect sting-related allergic reaction had an ICD-9 code indicating insect sting allergy.
Insect Sting-Related Reactions (continued)

- ICD-9 code identified patients were more likely to have a known allergy to insect stings.
- This group was more likely to have a duration of symptoms <1 hour.
- The ICD-9 identified group was more likely to have documentation of skin or cutaneous organ system involvement.
Discharge Instructions

Avoid offending allergen
Prescribed self-injectable epinephrine
Referred to an allergist

p=0.87
p=0.39
p=0.23

ICD-9 identified
Chart review identified
Implications

- Implementation of specific ICD-9 codes for food or insect sting allergies was *not* consistent across institutions.

- Although most insect sting allergy patients were identified by specific ICD-9 codes, nearly half food allergy patients would have been missed using specific ICD-9 codes alone.

- Furthermore, characteristics of patients with these reactions would have been distorted by including only patients identified by specific ICD-9 codes.
Multicenter Study of Emergency Department Visits for Food Allergy

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Food Allergy Case Identification

Patients identified by ICD-9 code:

- 693.1 (dermatitis due to food)
- 995.0 (other anaphylactic shock)
- 995.3 (allergy, unspecified)
- 995.60 (allergy due to unspecified food)
- 995.61-995.69 (allergy due to specified foods)
Data Collection

- **Structured chart review**
  - Demographic characteristics: Age, sex, race
  - Past medical & allergy history: Known allergy, asthma, concomitant medical problems
  - ED presentation: Signs & symptoms, duration of symptoms
  - Clinical course: Medications given in the ED, discharge medications

- **Potentially life-threatening reaction**
  - Two or more organ systems: cutaneous, respiratory, cardiovascular, gastrointestinal *OR*
  - Hypotension (systolic blood pressure <100 mmHg)
Food Allergy Results

- 678 patients with food allergy were randomly selected for chart review
- The cohort was 57% female and 43% white
- The mean age was 29 ± 18 years
- Only 41% of patients had documentation of a history of allergic reaction to the specific food that caused the current reaction
- 92% had documentation of a specific food item as the cause of the current reaction
### Specific Foods

<table>
<thead>
<tr>
<th>Food</th>
<th>Proportion</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crustaceans</td>
<td>19</td>
<td>16 – 22</td>
</tr>
<tr>
<td>Peanuts</td>
<td>12</td>
<td>9 – 14</td>
</tr>
<tr>
<td>Fruits and vegetables</td>
<td>12</td>
<td>10 – 15</td>
</tr>
<tr>
<td>Fish</td>
<td>10</td>
<td>8 – 12</td>
</tr>
<tr>
<td>Tree nuts</td>
<td>9</td>
<td>7 – 11</td>
</tr>
<tr>
<td>Milk</td>
<td>6</td>
<td>4 – 8</td>
</tr>
<tr>
<td>Eggs</td>
<td>2</td>
<td>1 – 4</td>
</tr>
<tr>
<td>Additives</td>
<td>1</td>
<td>0.5 – 2</td>
</tr>
<tr>
<td>Other food</td>
<td>36</td>
<td>33 – 40</td>
</tr>
</tbody>
</table>

* More than one option allowed
## Presentation and ED Course

<table>
<thead>
<tr>
<th></th>
<th>n=678</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrived by ambulance (%)</td>
<td>18</td>
<td>16 – 22</td>
</tr>
<tr>
<td>Duration of symptoms &lt;1 hour (%)</td>
<td>37</td>
<td>33 – 41</td>
</tr>
<tr>
<td>Treatment in the ED</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antihistamines (%)</td>
<td>72</td>
<td>68 – 75</td>
</tr>
<tr>
<td>Systemic steroids (%)</td>
<td>48</td>
<td>45 – 52</td>
</tr>
<tr>
<td>Respiratory treatments (%) *</td>
<td>33</td>
<td>29 – 37</td>
</tr>
<tr>
<td>Epinephrine (%)</td>
<td>16</td>
<td>13 – 19</td>
</tr>
<tr>
<td>Discharged to home (%)</td>
<td>97</td>
<td>95 – 98</td>
</tr>
</tbody>
</table>

* Respiratory treatments include inhaled β-agonists and inhaled anticholinergics
Given Discharge Instructions to Avoid Offending Allergen

Overall, 40% (95% CI, 36-43%)
Self-Injectable Epinephrine Prescription at Discharge

Overall, 16% (95% CI, 14-20%)
Referral to Allergist at Discharge

Overall, 12% (95% CI, 9-15%)
## Predictors of Receiving a Prescription for Self-Injectable Epinephrine at Discharge

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per ↑10 years)</td>
<td>0.9</td>
<td>0.8 – 1.2</td>
<td>0.59</td>
</tr>
<tr>
<td>Female</td>
<td>2.1</td>
<td>0.9 – 4.8</td>
<td>0.08</td>
</tr>
<tr>
<td>White race/ethnicity</td>
<td>2.8</td>
<td>1.2 – 6.5</td>
<td>0.02</td>
</tr>
<tr>
<td>Median household income (per ↑$10,000)</td>
<td>0.9</td>
<td>0.7 – 1.2</td>
<td>0.56</td>
</tr>
<tr>
<td>History of asthma</td>
<td>2.1</td>
<td>0.9 – 4.8</td>
<td>0.09</td>
</tr>
<tr>
<td>Peanuts as trigger</td>
<td>3.7</td>
<td>1.4 – 9.4</td>
<td>0.006</td>
</tr>
<tr>
<td>Epinephrine treatment in ED</td>
<td>3.9</td>
<td>1.8 – 8.6</td>
<td>0.001</td>
</tr>
<tr>
<td>ED visit volume (per ↑10,000 visits)</td>
<td>0.9</td>
<td>0.8 – 1.1</td>
<td>0.83</td>
</tr>
</tbody>
</table>
Food Allergy Summary

- Although allergic reactions to food can be life threatening, only 18% of patients came to the ED by ambulance and only 3% were admitted.
- A variety of foods provoked the allergic reaction with crustaceans and nuts being the most common.
- Only 16% of patients received a prescription for self-injectable epinephrine when leaving the ED.
- Similarly, only 12% were referred to an allergist as part of discharge instructions.
Multicenter Study of Emergency Department Visits for Insect Sting Allergies

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Carlos A. Camargo, Jr., MD, DrPH

Insect Sting Allergy Case Identification

Patients identified by ICD-9 code:

- 989.5 (toxic effects of venom)
- 995.0 (other anaphylactic shock)
- 995.3 (allergy, unspecified)
Type of Insect Sting Reaction

- "Local reactions" were considered to be reactions with skin rash, hives, or swelling confined to the area of the sting

- Mild systemic reactions involved a "generalized" component but could not be definitively classified as anaphylaxis

- Potentially life-threatening reaction
  - Two or more organ systems: cutaneous, respiratory, cardiovascular, gastrointestinal OR
  - Hypotension (systolic blood pressure <100 mmHg)
Insect Sting Severity Grade Classification

- **Mild**
  - Skin or cutaneous tissue involvement only

- **Moderate**
  - Anaphylaxis based on the involvement of two or more organ systems
  - Hypotension defined as a systolic blood pressure between 90 and 100 mmHg
  - No neurologic compromise

- **Severe**
  - Systolic blood pressure <90 mmHg or
  - Neurologic compromise (e.g., confusion, collapse, or loss of consciousness)
Insect Sting Allergy Results

- 617 patients with insect sting allergy underwent complete data abstraction

- 42% female and 61% white

- Mean age: $36 \pm 19$ years

- Only 32% of patients had documentation of a history of allergic reaction to insect stings

- 29% had documentation of another allergic problem
Current Episode

- Median number of stings was 1 (IQR, 1 to 1)
- 87% stung on only one part of the body
- Documented signs and symptoms
  - Skin: 86%
  - Respiratory: 22%
  - Gastrointestinal: 10%
  - Cardiovascular: 6%
- 358 (58%) had local reactions vs. 259 (42%) with systemic reactions
Severity Grade Classification

- Mild: 27%
- Moderate: 55%
- Severe: 18%
## Presentation and ED Course

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>Local</th>
<th>Mild systemic</th>
<th>Anaphylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrived by ambulance (%)</td>
<td>16</td>
<td>8</td>
<td>16</td>
<td>30</td>
</tr>
<tr>
<td>Stung within 6 hours of ED</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>arrival (%)</td>
<td>60</td>
<td>49</td>
<td>65</td>
<td>79</td>
</tr>
<tr>
<td>Treatment in the ED</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antihistamines (%)</td>
<td>57</td>
<td>48</td>
<td>71</td>
<td>68</td>
</tr>
<tr>
<td>Systemic steroids (%)</td>
<td>34</td>
<td>24</td>
<td>52</td>
<td>49</td>
</tr>
<tr>
<td>Respiratory treatments (%)</td>
<td>4</td>
<td>3</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Epinephrine (%)</td>
<td>6</td>
<td>2</td>
<td>9</td>
<td>13</td>
</tr>
<tr>
<td>Discharged to home (%)</td>
<td>97</td>
<td>98</td>
<td>92</td>
<td>97</td>
</tr>
</tbody>
</table>

* Respiratory treatments include inhaled β-agonists and inhaled anticholinergics
Given Discharge Instructions to Avoid Offending Allergen

Overall, 15% (95% CI, 11-20%)
Self-Injectable Epinephrine Prescription at Discharge

Overall, 27% (95% CI, 22-33%)
Referral to Allergist at Discharge

Overall, 20% (95% CI, 15-26%)
## Predictors of Receiving a Prescription for Self-Injectable Epinephrine at Discharge

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<tr>
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<th>Odds ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (per ↑5 years)</td>
<td>1.0</td>
<td>0.9 – 1.0</td>
<td>0.35</td>
</tr>
<tr>
<td>Stung within 6 hours of ED arrival</td>
<td>3.0</td>
<td>1.5 – 6.3</td>
<td>0.003</td>
</tr>
<tr>
<td>Known allergy to insect stings</td>
<td>3.5</td>
<td>2.0 – 6.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anaphylaxis (vs. mild systemic reaction)</td>
<td>1.9</td>
<td>1.1 – 3.3</td>
<td>0.02</td>
</tr>
<tr>
<td>Steroid treatment in ED</td>
<td>4.0</td>
<td>2.3 – 7.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Epinephrine treatment in ED</td>
<td>3.2</td>
<td>1.3 – 8.0</td>
<td>0.01</td>
</tr>
<tr>
<td>ED visit volume (per ↑10,000 visits)</td>
<td>1.0</td>
<td>0.9 – 1.0</td>
<td>0.22</td>
</tr>
</tbody>
</table>
Among patients with a systemic reaction (mild systemic or anaphylaxis), only 27% of patients received a prescription for self-injectable epinephrine when leaving the ED.

Strongest independent predictors of receiving a prescription for self-injectable epinephrine at ED discharge were a known allergy to insects and steroid treatment in the ED.

Similarly, only 20% were referred to an allergist as part of discharge instructions.
National Study of US Emergency Department Visits for Acute Allergic Reactions, 1993 to 2003

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Carlos A. Camargo, Jr., MD, DrPH

Methods

- Data obtained from the National Hospital Ambulatory Medical Care Survey (NHAMCS)
- Nationally representative sample of ED visits to non-institutional general & short stay hospitals
- 4-stage probability sampling frame covering
  - Geographic primary sampling units,
  - Hospitals within primary sampling units,
  - EDs within hospitals, and
  - Patients within EDs
- Medical record review of sampled patients
Methods

- ED visits for eleven years: 1993-2003
- Cases with a diagnosis of acute allergic reaction, including anaphylaxis were identified using ICD-9 codes:
  - 995.0 (other anaphylactic shock)
  - 995.1 (angioneurotic edema)
  - 995.2 (unspecified adverse effect of drug, medicinal and biological substance [due] to correct medicinal substance properly administered)
  - 995.3 (allergy, unspecified)
  - 995.6 (anaphylactic shock - adverse food reaction)
Results

- From 1993-2003 there were a total of 11.4 million allergy-related ED visits, representing:
  - 1.0% (95% CI, 0.97 – 1.12%), or
  - 1.04 million ED visits per year

- Number of allergy-related ED visits remained relatively stable from 1993 to 2003 (p for trend =0.79), with an average of 3.8 per 1,000 US population per year (95% CI, 3.4 – 4.1%)
Acute Allergic Reaction Trends
Results

- Demographic characteristics
  - Mean age: 35 years
  - Female: 64%
  - White race: 78%
  - Private insurance: 44%

- Although 63% of all visits were coded as urgent/emergent, only 3% required hospitalization

- 11% arrived to the ED by ambulance

- Only 1% of acute allergic reaction cases were coded as anaphylaxis
Acute Allergic Reaction Trends

Rate/1,000 US Population

Overall, Males, Females, Whites, Blacks

Results (continued)

- Medications were administered for 87% of visits
- Across 11-year period, prescribed medications were
  - H1 blockers 62% p for trend >0.05
  - Corticosteroids 37% p=0.02
  - H2 blockers 11% p=0.01
  - Epinephrine 11% p=0.02
  - β-agonists 3% p>0.05
- Only 53% of “anaphylaxis” cases received epinephrine, and 24% were admitted
Medication Trends

Percentage

- H1-blockers
- H2-blockers
- Corticosteroids
- Beta-agonists
- Epinephrine

Summary

- Acute allergic reactions account for >1 million ED visits each year
- Between 1993 and 2003, use of corticosteroids and H2 blockers increased but epinephrine usage was uncommon
- Only 1% of acute allergic reaction cases were coded as “anaphylaxis” (vs 30-50% expected)
- Among those with recognized “anaphylaxis” only half received treatment with epinephrine
Overall Summary

- Care must be taken when determining how cases of allergic reactions and anaphylaxis will be identified for research purposes.

- Although guidelines suggest specific approaches for the emergency management of food allergy and insect sting allergy, concordance with guidelines appears low.
Overall Summary (continued)

- At a minimum, there is poor documentation of medications prescribed at ED discharge

- Dissemination of guidelines for the emergency management of these disorders, and creation of systems to implement these guidelines are essential
Future Directions

- Compare ICD-9 code, clinical criteria, and chart review by a board-certified allergist (gold standard)
- Retrospective study assessing outcomes of patients after they leave the ED
- Prospective study
  - Consistent collection of data
  - Ability to collect biomarkers
  - Experience with acutely ill patients in preparation for trials
Thank you!