Update on Clinical Aspects of Anaphylaxis

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Case 1.0

- 7 year old girl with known peanut allergy
- Past history of anaphylaxis to peanut
- Carries an adrenaline autoinjector
- Has asthma on regular ICS and requires salbutamol approx once or twice every couple of months
- Currently has an URTI
- Has needed salbutamol bd last few days

Case 1.1

- At school; given a plain milk chocolate by a friend in a sealed wrapper
- Opens and eats the chocolate
- 45 minutes later develops a cough and watery eyes (playing on the grass oval)
- School gives salbutamol and calls mother who arrives and gives antihistamine

Case 1.2

- Mother takes her to Paediatric Emergency
- At triage noted to have a soft wheeze and O2 sats 98% in room air, RR 20, No tug/recession
- Nurse comments that "this is mild asthma not allergy because there is no rash or swelling"
- Waits 30 minutes for a doctor with ongoing cough and wheeze
- Mother asks if child should have adrenaline and is told no
- Doctor sees her and treats with salbutamol and steroids
- Symptoms resolve slowly over 24 hours

Case 1 Questions

- What is the diagnosis?
  - Asthma?
  - Anaphylaxis?
- What do you think was the most likely trigger for these symptoms?
- Do you agree/disagree with any advice or other aspects of management?

Case 2.0

- 9 year old boy
- No known history of any allergic disease
- Gets 'croup' about once a year – not requiring meds
- Eats tuna and avo sushi
  - 1 hour later
  - Sudden onset of cough and difficulty breathing
  - Mother observes him closely at home
  - Not given any treatment and recovers spontaneously over several hours
- Since then has eaten the same sushi meal without symptoms

Case 2.1

- What is the diagnosis?
- Which allergens, if any, should be tested?
- Does this child require an adrenaline autoinjector?
- Is any dietary avoidance required?

Case 2.2

- Could the sushi have been contaminated with an allergen?
  - But what?
  - Child has had an unrestricted diet for 9 years
- Or has he??
  - Never tried shellfish
  - Family doesn't eat shellfish
- SPT: Prawn 6x5 mm; Crab 7x6 mm

Case 2.3

- What is the diagnosis?
- Does this child require an adrenaline autoinjector?
- Is any dietary avoidance required?

DEFINITION OF ANAPHYLAXIS

- "a serious allergic reaction that is rapid in onset and may cause death"

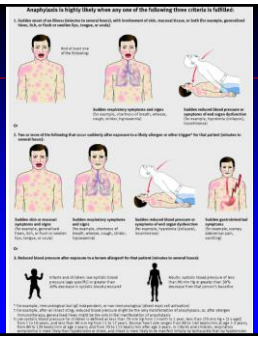
- Simons and Sheikh BMJ 2013; 346:f602

- Anaphylaxis is a rapidly evolving, generalised, multi-system reaction characterized by involvement of the respiratory and / or cardiovascular system and at least 1 other system such as the skin or gastrointestinal tract.

- Australasian Society of Clinical Immunologists and Allergists (ASCIA)
  - www.allergy.org.au

Sensitivity 97%
Specificity 82%

In ED:
NPV 98%
PPV 67%



Take home messages 1

- Anaphylaxis is on a continuum with mild / moderate allergic reactions
- Involves histamine (mediator) release from IgE dependent or independent mechanisms
- There are no “non-anaphylactic” histamine mediated reactions. There are just reactions that stop…..
- The diagnosis is Allergy not Anaphylaxis

EPIDEMIOLOGY OF ANAPHYLAXIS

Trends in hospitalizations for anaphylaxis, angioedema, and urticaria in Australia, 1993-1994 to 2004-2005

Loanne M. Poulos, BMedSc (Hons),* Anne-Marie Waters, Grad Dip Pop Hlth,* Patricia K. Correll, MPH,* Robert H. Loblay, PhD,† and Guy B. Marks, PhD* *Comparison and Indexes Australia* JACI. 2007

- ~3 fold increase in rate over 10 years

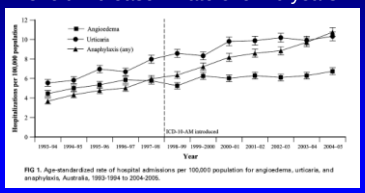
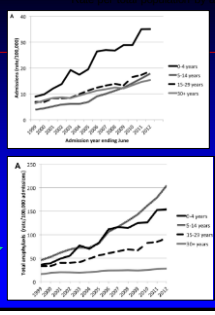


FIG 1. Age-standardized rate of hospital admissions per 100,000 population for angioedema, urticaria, and anaphylaxis, Australia, 1993-1994 to 2004-2005.

- Hospital anaphylaxis admission rates per 10^5 population:
  - 1998/99 = 6.3
  - 2004/05 = 10.6
  - 2005/06 = 12.2
  - 2011/12 = 17.7
  - 2013 = 19.2
- Rate of increase accelerating over time from 0.59/10^5/yr in 1998/99 to 1.11/10^5/yr in 2011/12.
- Increase of 8% per year from 1997 to 2013
- Rate of anaphylaxis admissions increasing as a proportion of total hospital admission i.e. not a product of increasing population.



Mullins et al. JACI 2015; 136(2):367

Mullins et al. CEA 2016; 1-12

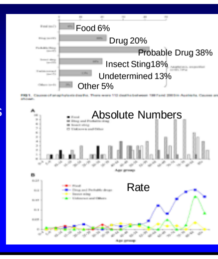
FATAL REACTIONS

Anaphylaxis fatalities and admissions in Australia

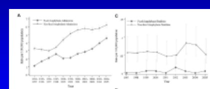
Woei Kang Liew, MBBS, MRCPCH, FAMS,[a,b] Elizabeth Williamson, MSc, PhD,[c,d] and Mimi L. K. Tang, MBBS, PhD, FRACP, FRCPA[a,d,e] *Melbourne, Australia, and Singapore*

2009:123:434-42.

- 112 fatalities over 9 years



- Admissions ↑ but fatalities static
- ? Due to improved management



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doi: 10.1111/cea.12748 — Clinical & Experimental Allergy, 1-12 — © 2016 John Wiley & Sons Ltd

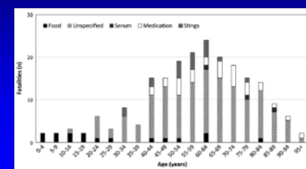
ORIGINAL ARTICLE Clinical Allergy

Increases in anaphylaxis fatalities in Australia from 1997 to 2013

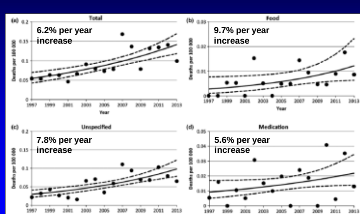
R. J. Mullins[1,2], B. K. Wainstein[3,4], E. H. Barnes[5], W. K. Liew[6] and D. E. Campbell[7,8]

[1]John James Medical Centre, Deakin, [2]Medical School, Australian National University, Canberra, ACT, [3]Sydney Children's Hospital, [4]School of Women's and Children's Health, University of New South Wales, [5]NHMRC Clinical Trials Centre, University of Sydney, Sydney, NSW, Australia, [6]SBCC Baby and Child Clinic, Gleneagles Medical Centre, Singapore, Singapore, [7]Children's Hospital Westmead, and [8]Discipline of Paediatrics and Child Health, University of Sydney, Sydney, NSW, Australia

- n = 324
  - Unspecified 205 (63%)
    - 50+% age > 60 yrs
  - Drug 52 (16%)
    - 85% > 50 yrs old
  - Insect Sting 41 (13%)
    - 80% > 50 yrs old
    - 95% male
  - Food 23 (7%)
    - 60% < 20 yrs old
  - Blood product 3 (1%)



Anaphylaxis Fatality Time Trends



Take home messages 2

- Anaphylaxis rates increasing over time
  - Hospital admissions
  - Fatalities
- Triggers for fatal anaphylaxis vary by age
  - Children / Adolescents = food
  - Adults = stings
  - Elderly = medication

CLINICAL FEATURES

Impact on quality of life

"It's not you—it's my anaphylaxis."

Evaluation of a Patient with a History of Anaphylaxis

- History
  - Signs and Symptoms of the event – ? c/w usual manifestations of anaphylaxis
  - Potential causes
    - Food; Sting; Drug; Exercise; Exposure
  - Duration of the episode(s)
  - Treatment required
  - Atopic status of the patient

Symptoms of Anaphylaxis

- Cutaneous (60 - 100%)
  - Urticaria (often explosive and rapidly progressive), angioedema, erythema, itch
- Upper respiratory (78%)
  - Nasal congestion, tongue swelling, hoarseness, stridor
- Lower respiratory (46 - 58%)
  - Cough, dyspnoea, wheeze, cyanosis
- GI Symptoms (4 - 37%)
  - Oral itch, Nausea, Vomiting, Diarrhoea
- Cardiovascular (25 - 30%)
  - Tachycardia, Arrythmia, Hypotension
- Neurological (5 - 27%)
  - Anxiety, 'Feeling of impending doom'

Must you have hives?

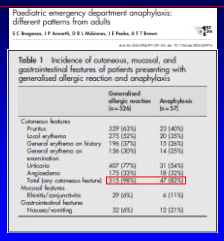
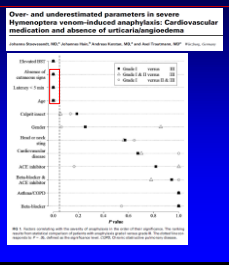

Paediatric emergency department anaphylaxis: different patterns from adults

Table 1 Incidence of cutaneous, mucosal, and gastrointestinal features of patients presenting with generalised allergic reaction and anaphylaxis

	Generalised allergic reaction (n = 526)	Anaphylaxis (n = 57)
Cutaneous features		
Pruritus	329 (63%)	23 (40%)
Local erythema	275 (52%)	20 (35%)
General erythema on history	196 (37%)	15 (26%)
General erythema on examination	156 (30%)	14 (25%)
Urticaria	407 (77%)	31 (54%)
Angioedema	175 (33%)	18 (32%)
Total (any cutaneous feature)	515 (98%)	47 (82%)
Mucosal features		
Rhinitis/conjunctivitis	29 (6%)	6 (11%)
Gastrointestinal features		
Nausea/vomiting	32 (6%)	12 (21%)


Over- and underestimated parameters in severe Hymenoptera venom-induced anaphylaxis: Cardiovascular medication and absence of urticaria/angioedema

Augmenting / Co-Factors




Take home message 3

- In order to get urticaria or angioedema you must
  - Be alive
  - Have a near normal blood pressure
  - Have a normal circulation
  - Not have vasoconstriction
- In severe anaphylaxis with circulatory compromise skin symptoms are often absent
- Beware of co-factors

PREDICTING THE RISK OF ANAPHYLAXIS

Anaphylaxis Risk: History

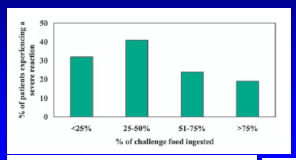
- Anaphylaxis is associated with previous anaphylaxis
- But anaphylaxis also frequently occurs after previous less severe reactions
  - Hourihane et al. Clin Exp Allergy. 1997 Jun;27(6):634-9

Anaphylaxis Risk: Clinical Predictors

- Asthma
  - ♦ Poor control increased risk
- Adolescents
- Nut allergy
- Mastocytosis
- Biochemical: Basal serum tryptase; PAF

Anaphylaxis Risk: Threshold Dose (Food)

- Anaphylaxis is associated lower threshold doses

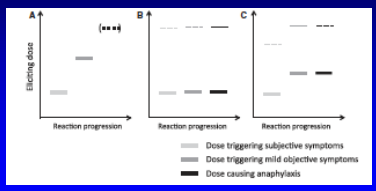


Risk of oral food challenges

Tamara T. Perry, MD, Elizabeth C. Matsui, MD, Mary K. Conover-Walker, CRNP, and Robert A. Wood, MD *Baltimore, Md*

J Allergy Clin Immunol 2004;114:1164-8.

Patterns of Reactions



Anaphylaxis Fatality Risk: Drugs

- ♦ **Risk Factors : Drug**
  - Antibiotics 35%
    - Penicillin 45%
    - Cephalosporins 48%
  - General Anaesthetic 35%
    - Muscle relaxants 72%
  - X-Ray Contrast 18%
- ♦ **Risk Factors : Patient**
  - Older Adults (Median age ~65 yrs)
  - Majority of deaths in a medical facility
  - Communication issues:
    - Unable to communicate d/t language or dementia or alert bracelet ignored
  - Co-morbid disease common
    - 40% asthma/emphysema
    - 74% CVS disease

Anaphylaxis Fatality Risk: Insect Sting

- **Risk Factors : Insect**
  - ♦ Honeybee 72%
  - ♦ Ant 9%
  - ♦ Tick 9%
  - ♦ Wasp 6%
- **Risk Factors : Patient**
  - ♦ Male 90%
  - ♦ Adults (Median age 50 yrs)
- **Risk Factors : Location**
  - ♦ Death often occurs at home or in rural location
    - May represent delayed presentation and treatment
- **Risk Factors : Activity**
  - ♦ Tending or disturbing hives; driving
- **Risk Factors : Management**
  - ♦ Manual attempts at tick removal (3 tick deaths in Aus series)
  - ♦ Sudden CVS collapse after assuming upright posture
  - ♦ Adrenaline autoinjector not prescribed or used when prescribed
  - ♦ No previous immunotherapy in nearly all cases

Anaphylaxis Fatality Risk: Food

- **Risk Factors : Patient**
  - Young adults and children (median age 28 yrs)
  - Asthma in majority. Often poorly controlled or compliant
  - Previous reactions often mild
  - Lapses in vigilance due to disrupted routine (unaware of allergen in food)
  - Low rate of allergy specialist reviews prior to death
  - Ethanol or recreational drugs
  - Most have known food allergy / History of mild reactions
- **Risk Factors : Trigger**
  - Seafood - Australia
  - Peanut/Tree nuts – Australia / USA / UK
  - Cow's Milk – UK / Israel
- **Risk Factors : Source**
  - Eating outside the home incl school, preschool, work, restaurants
- **Risk Factors : Management**
  - Sudden CVS collapse in patients assuming upright posture (e.g. to sit in a car)
  - Delayed treatment with adrenaline
    - Autoinjector not prescribed or used
    - Adrenaline not given in ambulance

Take home messages 4

- Milder reactions often precede anaphylaxis
- Asthma control important
  - Incl not overusing LABA's
- Threshold dose is important
- Co-morbidity assoc with fatalities in drug anaphylaxis
- Upright posture and delayed adrenaline assoc with fatalities in food and venom

MANAGEMENT

Management of Acute Anaphylaxis

- ABC
- Adrenaline
  - **1st line treatment**
  - Dose 1:1000 0.01 ml / kg; IMI; q5min
  - IMI anterolateral thigh > IMI or SC deltoid
    - Absorption better & plasma levels higher in healthy adults
  - Infusion (IV bolus NOT recommended)
    - Reserved for arrest or profound hypotension despite repeated IMI adrenaline

ascia
www.allergy.org.au

Guidelines

Acute management of anaphylaxis

These guidelines are intended for primary care physicians and nurses providing first responder emergency care.

Anaphylaxis definition

Any **acute onset illness** with **typical skin features** (urticarial rash or erythema/flushing, and/or angioedema), **PLUS** involvement of **respiratory** and/or **cardiovascular** and/or persistent severe **gastrointestinal** symptoms.
OR
Any **acute onset** of **hypotension** or **bronchospasm** or **upper airway obstruction** where anaphylaxis is considered possible, **even if typical skin features are not present**.

Signs and symptoms of allergic reactions

Mild or moderate reactions
- Swelling of lips, face, eyes
- Hives or welts
- Tingling mouth
- Abdominal pain, vomiting (these are signs of anaphylaxis for insect allergy)

Anaphylaxis
Watch for any one of the following signs of anaphylaxis:
- Difficult/noisy breathing
- Swelling of tongue
- Swelling/tightness in throat

Adrenaline Autoinjectors

EpiPen

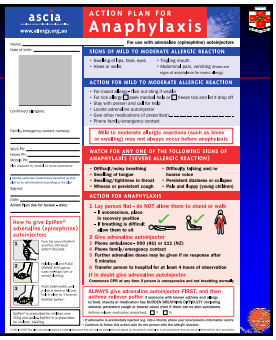
Autoinjector Prescribing

- All patients entitled to 2 autoinjector devices regardless of age
- Dose
  - ♦ EpiPen Jr (150ug) for 10 - 20 kg
  - ♦ EpiPen (300 ug) for > 20 kg
  - ♦ Dose calculation = 10 ug/kg adrenaline
  - ♦ ASCIA Prescribing Guidelines
    - https://www.allergy.org.au/health-professionals/anaphylaxis-resources/adrenaline-autoinjector-prescription
- Different to product information (> 30 kg)
- Additional authority prescription if used or expired
- Over the counter

ASCIA Anaphylaxis Action Plans

2017 Changes
- Bold symptoms of anaphylaxis
- Guidance re positioning of the patient
- Change to hold time for EpiPen
- Guidance for asthma versus anaphylaxis

2018 Changes
- Tick boxes for tick allergy
- Action plan due for review date
- EpiPen dose guide lower left corner
- Action if adrenaline accidentally injected lower right


ascia
www.allergy.org.au
ACTION PLAN FOR
Anaphylaxis
For use with adrenaline (epinephrine) autoinjectors
SIGNS OF MILD TO MODERATE ALLERGIC REACTION
ACTION FOR MILD TO MODERATE ALLERGIC REACTION
WHO to moderate allergic reactions (such as hives or swelling) may not always occur before anaphylaxis
WATCH FOR ANY ONE OF THE FOLLOWING SIGNS OF ANAPHYLAXIS (SEVERE ALLERGIC REACTION)
ACTION FOR ANAPHYLAXIS
How to give EpiPen® adrenaline (epinephrine) autoinjectors
ALWAYS give adrenaline autoinjector FIRST, and then asthma reliever puffer

Take home messages 5

- Adrenaline is first line treatment for anaphylaxis
- Should be administered IMI
- 300mcg autoinjector for all humans over 20kg
- Autoinjector should be carried at all times
- All patients must be provided with an ASCIA action plan and be trained in autoinjector use
  - ♦ **Brand Specific**
- Management guidelines available online

THANK YOU

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