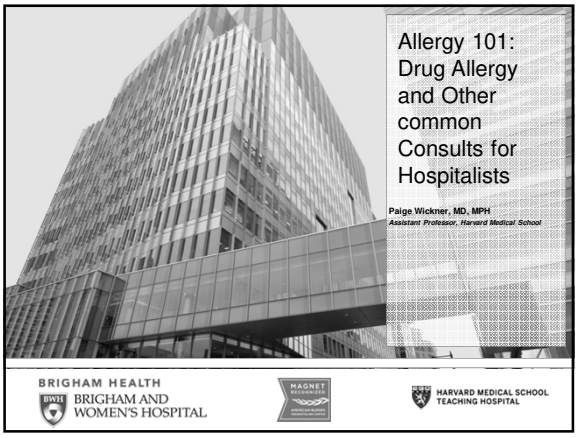


Allergy 101: Drug Allergy and Other common Consults for Hospitalists

Paige Wickner, MD, MPH
Assistant Professor, Harvard Medical School

BRIGHAM HEALTH
BRIGHAM AND WOMEN'S HOSPITAL
HARVARD MEDICAL SCHOOL TEACHING HOSPITAL

Disclosures

BRIGHAM AND WOMEN'S Health Care

- Dual employment, VP of Safety at CVS Health, nothing discussed today relevant to role at CVS Health

Outline

BRIGHAM AND WOMEN'S Health Care

I. Drug allergies
   I. Beta lactam
   II. Sulfa
   III. NSAIDs
   IV. COVID-19 vaccines
II. Anaphylaxis

CASE 1: Drug Allergy

BRIGHAM AND WOMEN'S Health Care

- 82 y.o. female admitted with pneumonia.
- She has a listed allergy to Penicillin and needs antibiotics
- Patients EMR says:
  - Allergy to Penicillin, reaction unknown
  - Allergy to shellfish, reaction anaphylaxis
  - Allergy to dust

Question set 1: Drug allergy basics

BRIGHAM AND WOMEN'S Health Care

- What questions should I ask to clarify a listed allergy that says 'reaction-unknown'?
- Is there a role for skin testing in the inpatient setting? How do you choose the patients to skin test?
- Can hospitalists skin test?

Drug allergy: History in 3 minutes

BRIGHAM AND WOMEN'S Health Care

- Best time to clarify drug allergies…
- Name of medication
- Indication
- Timing of reaction in relation to taking med
- Nature of reaction
  - ?Blistering
  - ?Mucosal involvement
  - End organ damage
- Similar agents tried
- Alternative options

Who should have a skin test?

BRIGHAM AND WOMEN'S Health Care

- Penicillin allergy with type I characteristics, delayed rash, distant allergy, prior to BMT or organ transplant
- Skin testing NOT recommended for SJS, TEN, serum sickness, cytotoxic reaction, non immunologic adverse drug effects
- Can NOT test patients on antihistamines (H1 or H2)
- State by state rules vary on requirement to oversee testing: allergists, pharmacists, RN, NP, trained MDs

Challenge vs. Desensitization

BRIGHAM AND WOMEN'S Health Care

Challenge/Test dose

- Confirms low suspicion cases
- After negative skin tests when possible
- Often involves 1/10 dose→ observation→ remainder of dose
- If passed, patient is considered not allergic
- Performed in allergists office or on floor of hospital

Desensitization

- Used to allow the patient to TEMPORARILY take the drug in question
- Used for immediate type reactions and when have no acceptable alternative agent
- Compliance important
- MICU
- Higher risk of anaphylaxis

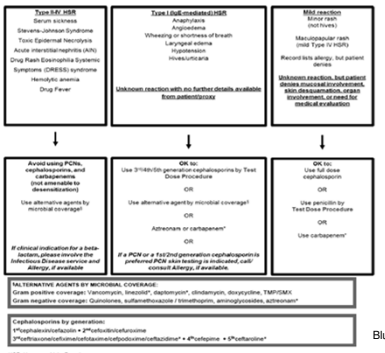
Question set 2: Beta lactam allergy

BRIGHAM AND WOMEN'S Health Care

- If no skin testing is available…what can I do?
- Can I give a cephalosporin in a patient with a penicillin allergy?
- What about patients with a listed allergy to a cephalosporin? Can I give a different generation cephalosporin?
- When do I need to call allergy?

PCN Hypersensitivity Pathway 2019

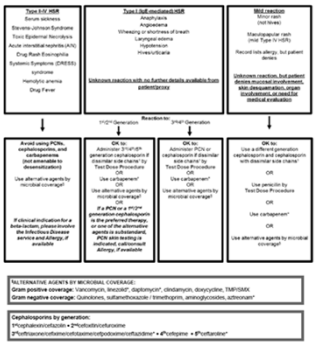
BRIGHAM AND WOMEN'S Health Care



Blumenthal, et al Ann Allergy Clin Immunol 2015
Blumenthal…Wickner. ICHE 2019.

Cephalosporin Hypersensitivity Pathway 2019

BRIGHAM AND WOMEN'S Health Care



Cephalosporins in patients w/ PCN allergy

BRIGHAM AND WOMEN'S Health Care

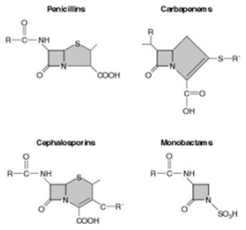
- Not straightforward- if you have an allergy consult service, utilize it
- Macy et al April 2021 JAMA Network- removed cross reactivity warning in PCN allergic patients >4million studied, no safety issues identified, increased cephalosporin use
- For patients with mild cutaneous reactions without features of immediate allergy UpToDate recommends:
  - Usually ok to give 3rd/4th generation cephalosporin
  - Ok to give a carbapenem
  - Ok to give aztreonam
  - Give 1st/2nd generation cephalosporins or penicillins via test dose

Blumenthal K & Solensky R. Choice of antibiotics in penicillin-allergic hospitalized patients.UpToDate. Accessed on Sept 2021

Aztreonam

BRIGHAM AND WOMEN'S Health Care

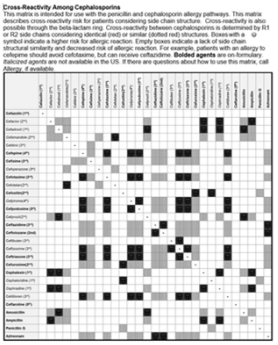
- Very little cross-reactivity due to its low immunogenic potential
- A safe alternative for PCN allergic patients
- Cross-reactivity exists with Ceftazidime
  - Identical side chain to Aztreonam



Slide courtesy of Mariana Castells

Cephalosporin cross reactivity

BRIGHAM AND WOMEN'S Health Care



When to call allergy (if available):

BRIGHAM AND WOMEN'S Health Care

- Skin testing needed
- Multiple beta lactam allergy
- The patient has a proven allergy to the medication and for antibiotics infectious disease agrees that it is the best and only first line therapy
- You want to give a medication that the patient has had a severe delayed reaction to:
  - SJS
  - TEN
  - DRESS
  - Drug induced organ damage
  - Serum sickness

What if there is no allergy to call!!

BRIGHAM AND WOMEN'S Health Care

- Avoidance if possible
- Consult literature/resources
- Develop standard hospital approaches for common allergens that don't rely on specialist
  - Beta lactams
  - Contrast allergy
  - NSAIDs
- Refer to allergy as an outpatient

Case 1: Allergy available

BRIGHAM AND WOMEN'S Health Care

- Obtain history
- Graded challenge when appropriate
- Skin testing performed, if negative challenge performed, allergy deleted from record forever (90-99% success rate)
- Desensitization if patient too sick for skin testing and penicillin/cephalosporin best agent

Case 1: NO allergy available

BRIGHAM AND WOMEN'S Health Care

- Get history
- Options are:

-Use alternative agent

- Graded dose challenge or ok to proceed depending on agent
- Send to allergy at D/C

Case 1: Questions

BRIGHAM AND WOMEN'S Health Care

Patients EMR says:

- Allergy to Penicillin, reaction unknown
- Allergy to shellfish, reaction anaphylaxis
- Allergy to dust

- Can she have a COVID19 vaccine?
- Can she have contrast?

Screening Questionnaire/Risk

BRIGHAM AND WOMEN'S Health Care

1.Did your reaction occur in the past 12 months? Y N

2. Did your reaction involve any systemic symptoms other than a rash (wheezing, shortness of breath, throat closing, nausea, diarrhea, vomiting, or other symptoms including passing out or loss of consciousness) or other skin symptoms? If unknown mark NO Y N

3. Was your reaction life threatening (ie severe anaphylaxis, requiring epinephrine, emergency room visit, hospitalizations)? If unknown mark NO Y N

4. Are you pregnant? Y N

5. Did your reaction cause skin blisters or skin peeling, or any ulcers of the lining or your mouth, eyes or genitals OR were you diagnosed with SJS (Stevens Johnson syndrome) or TEN (toxic epidermal necrolysis)?? If unknown mark NO Y N

6. Did your reaction cause any organ damage such as liver inflammation/hepatitis, kidney damage/failure/dialysis, severe joint pain/swelling, serum sickness, or DRESS (drug reaction with eosinophilia)? If unknown mark NO Y N

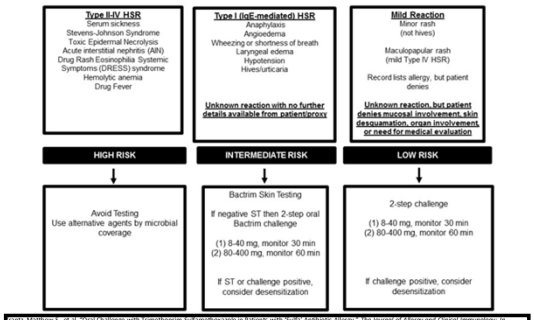
Recommendations

BRIGHAM AND WOMEN'S Health Care

- LOW RISK: Direct 2 step oral amoxicillin challenge (50mg amoxicillin, monitor 30min then 500mg amoxicillin then monitor 60min)
  - Non urticarial, non blistering rash (benign rash)
  - GI symptoms
  - Headaches
  - Other benign somatic symptoms
  - Unknown history
  - IgE cutaneous symptoms >5 years ago
- High RISK : Skin testing first with penicillin if:
  - Reaction in the past 12 months (but DO NOT TEST ANAPHYLAXIS<1 year)
  - shortness of breath with penicillin
  - anaphylaxis or systemic IgE symptoms
  - Previous positive PCN skin testing
  - Pregnancy
- DON'T TEST:
  - Blistering rash
  - Hemolytic anemia, Nephritis, Hepatitis
  - Lab abnormality associated with penicillin use

Bactrim Hypersensitivity Pathway

BRIGHAM AND WOMEN'S Health Care



Trantz, Matthew S., et al. "Oral Challenge with Trimethoprim-Sulfamethoxazole in Patients with "Sulfa" Antibiotic Allergy." *The Journal of Allergy and Clinical Immunology: In Practice*, 2019, doi:10.1016/j.jaip.2019.07.003.

HSR: Hypersensitivity Reaction

Sulfa allergy

BRIGHAM AND WOMEN'S Health Care

For patients with morbilliform rash without fever or other severe cutaneous symptoms (SJS etc) can be done as outpatient or inpatient and does not require ICU

Bactrim (Sulfamethoxazole 200mg-Trimethoprim 40 mg/5mL)				
Day	Time	Trimethoprim Dose (mg)	Sulfamethoxazole Dose (mg)	Volume and formulation
1	9am	0.8mg	4mg	0.1 mL oral suspension
	11am	1.6mg	8mg	0.2mL oral suspension
	1pm	4mg	20mg	0.5mL oral suspension
	5pm	8mg	40mg	1mL oral suspension
2	9am	16mg	80mg	2mL oral suspension
	3pm	32mg	160mg	4mL oral suspension
	9pm	40mg	200mg	5mL oral suspension
3	9am	80mg	400mg	1 single strength tablet
4 onward	9am	80mg	400mg	1 single strength tablet

Case 2: NSAID allergy

BRIGHAM AND WOMEN'S Health Care

- MI is a 65 yo male with obesity, hypercholesterolemia and diabetes admitted with chest pain and concerning EKG findings for MI
- The team would like to give him aspirin
- He has a listed allergy to 'NSAIDs', listed reaction- hives.

* Question #2

BRIGHAM AND WOMEN'S Health Care

- The safest immediate choice is:
  a. skin test to NSAIDs
  b. figure it out post catheterization
  c. avoid aspirin
  d. desensitize
  d. start opiate for pain given listed allergy

* Question #2

BRIGHAM AND WOMEN'S Health Care

- The safest immediate choice is:
  a. skin test to NSAIDs
  b. figure it out post catheterization
  c. avoid aspirin
  d. desensitize
  d. start opiate for pain given listed allergy

NSAID allergy pearls

BRIGHAM AND WOMEN'S Health Care

- No skin testing available
- Cross reactivity- always assume cross reactivity even if reaction to one NSAID
- Celebrex usually OK, most reactions to COX-1 inhibition
- Avoidance list
- Call allergy if available, if not, admit to ICU with 1:1 nursing, epi IM and Benadryl at bedside and desensitize

* Question #3

BRIGHAM AND WOMEN'S Health Care

- You are caring for a 45 yo female who has moderate knee pain during her admission. Rheumatology recommends an NSAID however she has a listed allergy to ibuprofen and aspirin with reaction anaphylaxis.
  The safest immediate choice is:
  a. skin test to NSAID
  b. start celecoxib
  c. start naproxen
  d. start opiate for pain given listed allergy

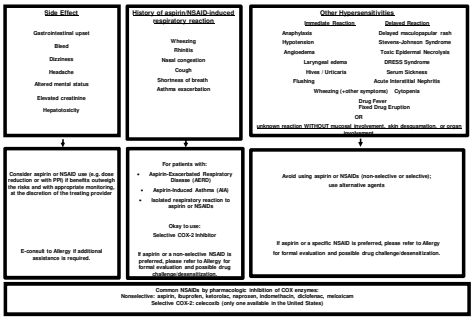
* Question #3

BRIGHAM AND WOMEN'S Health Care

- You are caring for a 45 yo female who has moderate knee pain during her admission. Rheumatology recommends an NSAID however she has a listed allergy to ibuprofen and aspirin with reaction anaphylaxis.
  The safest immediate choice is:
  a. skin test to NSAID
  b. start celecoxib
  c. start naproxen
  d. start opiate for pain given listed allergy

Aspirin/NSAID Hypersensitivity Pathway

BRIGHAM AND WOMEN'S Health Care



Avoidance list

BRIGHAM AND WOMEN'S Health Care

Aspirin or salicylate-containing medications
- *Exedrine*
- *Pepto- Bismol*
- *Alka-Seltzer*
- *Aggrenox*
- *Anacin*
- *Arthropan*
- *Ascriptin*
- *Asperbuf*
- *Aspergum*
- *Aspermin*
- *Aspir-Mox*
- *Aspirtab*

Ibuprofen
- *Motrin*
- *Advil*

Naproxen
- *Aleve*
- *Anaprox*

Salsalate
- *Amigesic*
- *Salflex*
- *Argesic*

Flurbiprofen
- *Ansaid*

Ketorolac
- *Toradol*

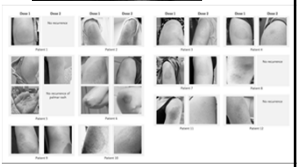
Diclofenac
- *Arthrotec*

https://aerd.partners.org/

Vaccine allergies

BRIGHAM AND WOMEN'S Health Care

- mRNA vaccines with unique ingredients unrelated to key allergens from other vaccines (gelatin, egg, latex)
- Frequent side effects of COVID 19 vaccines, confusing re: side effects vs. allergic reactions- very rare for either to be contraindication to second dose
- Rare severe allergic reactions
- Localized cutaneous manifestations more common
- Poor utility of skin testing so far
- Almost everyone able to safely complete second dose of COVID-19 vaccination



Robinson et al. Incidence of Cutaneous Reactions After Messenger RNA COVID-19 Vaccines. JAMA Dermatol. 2021

Blumenthal et al. Delayed Large Local Reactions to mRNA-1273 Vaccine against SARS-CoV-2. NEJM 2021

Vaccine allergies cont.

BRIGHAM AND WOMEN'S Health Care

Table 2. Anaphylaxis Cases After mRNA COVID-19 Vaccination (n = 16)

Characteristics	No. (%)		
	Both mRNA vaccines (n = 16)	Pfizer-BioNTech (n = 7)	Moderna (n = 9)
Age, mean (SD), y	41 (13)	41 (14)	41 (13)
Female	15 (94)	6 (86)	9 (100)
Prior allergic reactions	10 (63)	3 (43)[a]	7 (78)[a]
Prior anaphylaxis	5 (31)	1 (14)	4 (44)
Symptoms			
Pruritus, urticaria, and/or angioedema	14 (88)	6 (86)	8 (89)
Sensation of throat closure, cough, wheeze, and/or dyspnea	14 (88)	6 (86)	8 (89)
Hypotension and/or tachycardia	7 (44)	3 (43)	4 (44)
Nausea, vomiting, and/or diarrhea	8 (50)	3 (43)	5 (56)
Minutes to onset, mean (SD) [range]	17 (28) [1-120]	14 (7) [10-30]	19 (38) [1-120]
Symptom timing			
≤15 min	14 (88)	6 (86)	8 (89)
≤30 min	15 (94)	7 (100)	8 (89)
Received epinephrine	9 (56)	6 (86)	3 (33)
Treatment setting[b]			
Emergency department	9 (56)	4 (57)	5 (56)
Hospitalization	1 (6)	1 (14)	0
Intensive care unit	1 (6)	1 (14)	0
Brighton level[c]			
1	1 (6)	0	1 (11)
2	13 (81)	7 (100)	6 (67)
3	2 (13)	0	2 (22)
NIAID/FAAN criteria[d]	9 (56)	4 (57)	5 (56)
Severity[e]			
Grade I	7 (44)	3 (43)	4 (44)
Grade II	9 (56)	4 (57)	5 (56)
Grade III	0	0	0
Grade IV	0	0	0
Elevated tryptase[a]	1 (6)	0	1 (11)

Blumenthal et al. JAMA 2021

CASE 3: Anaphylaxis

BRIGHAM AND WOMEN'S Health Care

- 20 yo male with peanut allergy admitted for nephrolithiasis
- Day 2 of his admission he takes a bite of a peanut butter sandwich. Within minutes eating, he develops hives, sensation of throat closing, ocular swelling, and chest discomfort.

Question set 3: Anaphylaxis

BRIGHAM AND WOMEN'S Health Care

- How do I know if its really anaphylaxis?
- How do I treat anaphylaxis?
- What are the options to prescribe epinephrine for discharge to patients who need it?

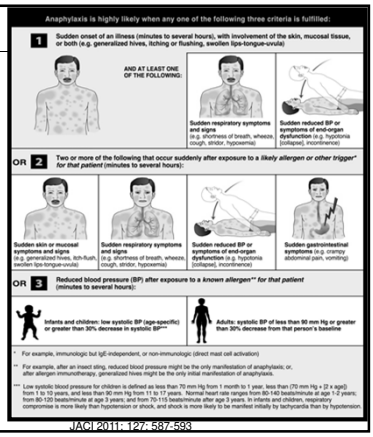
Is it really anaphylaxis?

BRIGHAM AND WOMEN'S Health Care

Here's my advice…..

With rare exception, If you think its anaphylaxis, treat it as anaphylaxis, then analyze after the fact.

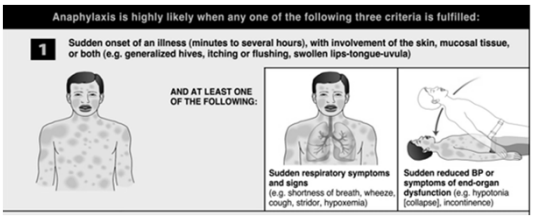
Anaphylaxis



JACI 2011; 127: 587-593

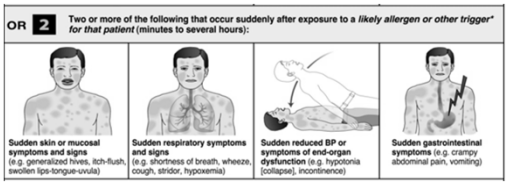
Strictest criteria

BRIGHAM AND WOMEN'S Health Care



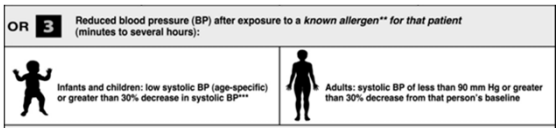
Likely exposure criteria

BRIGHAM AND WOMEN'S Health Care



Exposure to patient known allergen

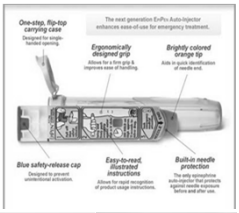
BRIGHAM AND WOMEN'S Health Care



Anaphylaxis: Treatment

BRIGHAM AND WOMEN'S Health Care

- Epi, Epi, Epi
  1:1000=1mg/ml
- dose 0.3-0.5mg in adults
- route of administration
  IM in anterolateral thigh
- Code cart differences:
  1:10,000=0.1mg/ml
- Second dose: 16-36%
- Biphasic reaction:
  3-20%



Si [illegible] 361: 166.671-675

Anaphylaxis: Treatment cont

BRIGHAM AND WOMEN'S Health Care

- O2 for hypoxemia
- Inhaled beta 2 agonists for refractory bronchospasm (nebulizer)
- IVF for refractory hypotension
- H1/H2 antagonists
- Corticosteroids- poor data this helps acutely
- **Stop offending agent** (if its during ingestion, infusion etc)

The epinephrine IM delivery options

BRIGHAM AND WOMEN'S Health Care

Case 3: follow up

BRIGHAM AND WOMEN'S Health Care

- Given Epi 0.3mg IM x1, cetirzine, and solumedrol.
- Monitored vital signs and symptoms x 2 hours
- Reviewed epinephrine use and carrying portable epinephrine
- Reviewed ingredients of frappe, chocolate included, EMR didn't connect with our nutrition database properly

*Question #3

BRIGHAM AND WOMEN'S Health Care

- The correct dose of epinephrine for use in anaphylaxis is:
  a. 0.6mg 1:1000 IM thigh
  b. 0.3mg 1:1000 IM thigh
  c. 0.3mg 1:10,000 IM thigh
  d. 0.3mg 1:1000 IV

*Question #3

BRIGHAM AND WOMEN'S Health Care

- The correct dose of epinephrine for use in anaphylaxis is:
  a. 0.6mg 1:1000 IM thigh
  b. 0.3mg 1:1000 IM thigh
  c. 0.3mg 1:10,000 IM thigh
  d. 0.3mg 1:1000 IV

Conclusions

BRIGHAM AND WOMEN'S Health Care

- Know what questions to ask to clarify drug allergies
- Think about designing systems for common allergies whether or not your hospital has allergy services
- Know when to call an allergist
- Review anaphylaxis