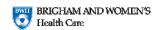


Disclosures



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

Outline



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





CASE 1: Drug Allergy



- 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



- 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?



- 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



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

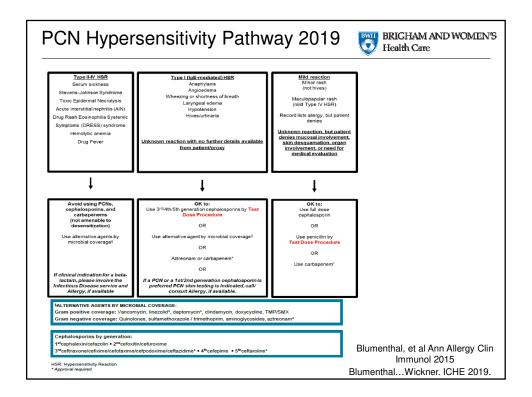
Desensitization

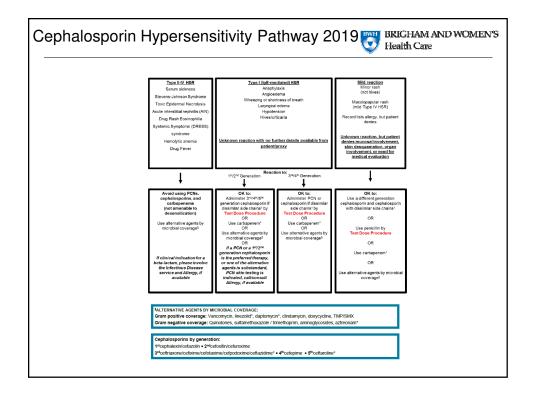
- Used to allow the patient to TEMPORARILY take the drug in question
- Used for immediate type reactions and when have no acceptable alternative agent
- Compliance important
- MICU
- Higher risk of anaphylaxis

Question set 2: Beta lactam allergy



- 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?





Cephalosporins in patients $\ensuremath{w/}\xspace$ PCN allergy



- 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 cephalosporing
 - Ok to give a carbapenem
 Rhymenthal K & Solensky
 - Ok to give aztreonam

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

 Give 1st/2nd generation cephalosporins or penicillins via test dose

Aztreonam

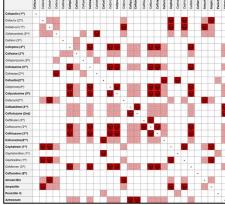


- Very little cross-reactivity due to its low immunogenic potential
- A safe alternative for PCN allergic patients
- <u>Cross-reactivity exists with</u> <u>Ceftazidime</u>
 - Identical side chain to Aztreonam

Cephalosporin cross reactivity



Fores-Reactivity Among Cephalosporins
This matrix intended for use with the penicilin and cephalosporin ellergy pathways. This matrix
describes cross-sendinyl this for patients considering side chain shudure. Cross-reactivity is also
describes cross-length with the penicilin and cephalosporin ellergy pathways. This matrix
describes cross-length with the penicilin and cephalosporin ellergy than the considering development of the co



When to call allergy (if available): BRIGHAM AND WOMEN'S Health Care

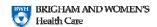
- · Skin testing needed
- Multiple beta lactam allergy
- The patient has a proven allergy to the medication and for antibiotics infectious disease agrees that it is the best and only first line therapy
- You want to give a medication that the patient has had a severe delayed reaction to:
 - SJS
 - TEN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



- 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



- 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



Patients EMR says:

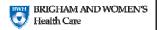
- Allergy to Penicillin, reaction unknown
- Allergy to shellfish, reaction anaphylaxis
- Allergy to dust
- Can she have a COVID19 vaccine?
- Can she have contrast?

Screening Questionnaire/Risk



- 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

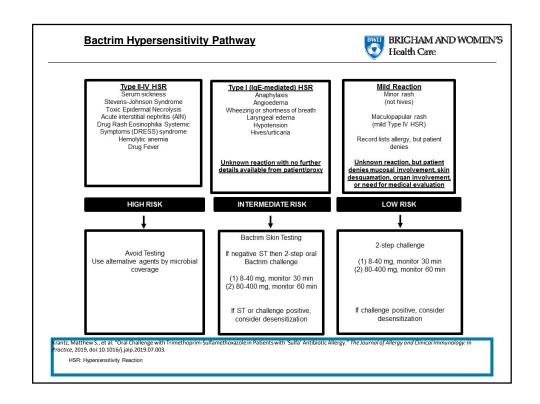


- LOW RISK: Direct 2 step oral amoxicillin challenge (50mg amoxicillin, monitor 30min then 500mg amoxicillin then monitor 60min)
 - Non urticarial, non blistering rash (benign rash)
 - GI symptoms
 - Headaches
 - Other benign somatic symptoms
 - Unknown history
 - IgE cutaneous symptoms >5 years ago

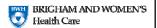
- High RISK : Skin testing first with penicillin if:
 - Reaction in the past 12 months (but DO NOT TEST ANAPHYLAXIS<1 year)
 - shortness of breath with penicillin
 - anaphylaxis or systemic IgE symptoms
 - Previous positive PCN skin testing
 - Pregnancy

· DON'T TEST:

- Blistering rash
- Hemolytic anemia, Nephritis, Hepatitis
- Lab abnormality associated with penicillin use



Sulfa allergy



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



- 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



- · 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



- · 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



- 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



 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



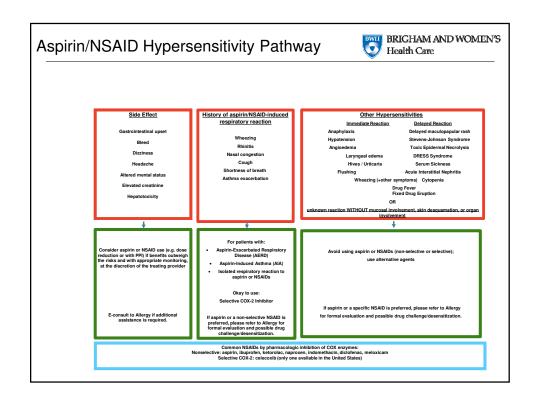
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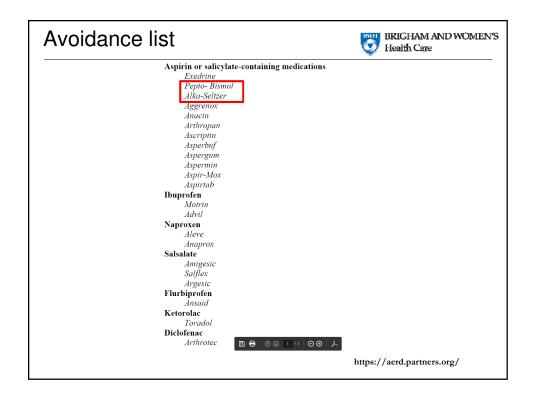
The safest immediate choice is:

a. skin test to NSAID

b. start celecoxib

- c. start naproxen
- d. start opiate for pain given listed allergy





Vaccine allergies



- 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.



	No. (%)			
Characteristics	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) ^b	
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 ^c				
Emergency department	9 (56)	4 (57)	5 (56)	
Hospitalization	1(6)	1 (14)	0	
Intensive care unit	1(6)	1 (14)	0	
Brighton level ^d				
1	1(6)	0	1(11)	
2	13 (81)	7 (100)	6 (67)	
3	2 (13)	0	2 (22)	
NIAID/FAAN criteria®	9 (56)	4 (57)	5 (56)	
Severity ^f				
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 ^g	1(6)	0	1(11)	

Blumenthal et al. JAMA 2021

CASE 3: Anaphylaxis



- 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



- · 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?

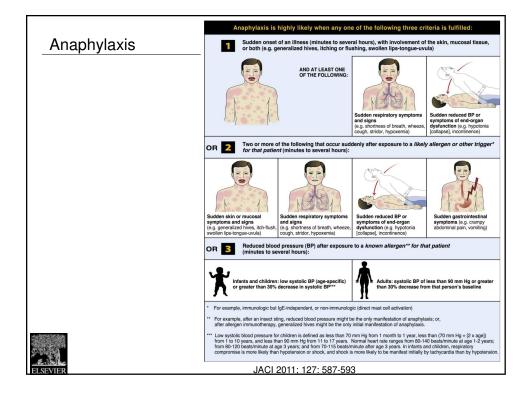


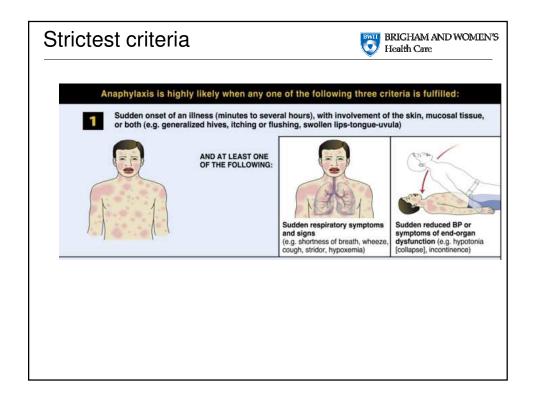
Here's my advice.....

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

TO DO LIST

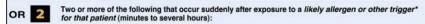
Follow Op Follow Op . . .





Likely exposure criteria







Sudden skin or mucosal symptoms and signs (e.g. generalized hives, itch-flush, swollen lips-tongue-uvula)



and signs
(e.g. shortness of breath, wheeze, cough, stridor, hypoxemia)



symptoms of end-organ dysfunction (e.g. hypotonia [collapse], incontinence)



symptoms (e.g. crampy abdominal pain, vomiting)

Exposure to patient known allergen







Reduced blood pressure (BP) after exposure to a *known allergen** for that patient* (minutes to several hours):



Infants and children: low systolic BP (age-specific) or greater than 30% decrease in systolic BP***



Adults: systolic BP of less than 90 mm Hg or greater than 30% decrease from that person's baseline

Anaphylaxis: Treatment



- Epi, Epi, Epi1:1000=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%





Anaphylaxis: Treatment cont



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



Case 3: follow up



- 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



 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



 The correct dose of epinephrine for use in anaphylaxis is:

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c. 0.3mg 1:10,000 IM thigh

d. 0.3mg 1:1000 IV

Conclusions



- 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