

Disclosures



 Dual employment, VP of Enterprise Patient Safety at CVS Health. Nothing discussed today relevant to role at CVS Health

Outline



- I. Drug allergies
 - I. Basics
 - II. Beta lactam
 - III. Sulfa
 - IV. Fluoroquinolones
 - V. Contrast allergy
- II. Immunodeficiency
- III. Anaphylaxis



Hypothetical Case Example #1



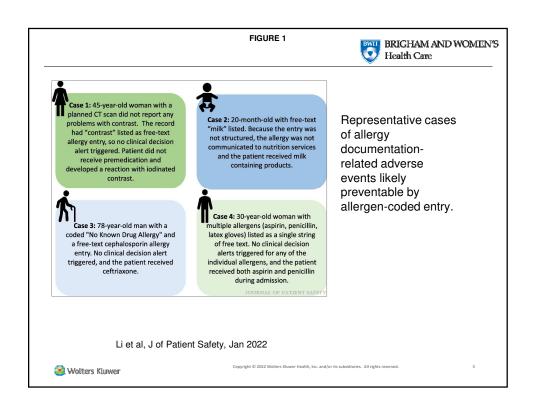
- D.L. is a 61 yo female with multiple drug allergies.
- This is her allergy list:

Allergen	Reaction	Severity	Free text
Codeine	Mental status change	Medium	
Penicillins			Hives
Bactrim	Rash	Medium	
Zolpidem			She felt really odd

Hypothetical Case Example #1



- She unfortunately gets a post viral pneumonia requiring antibiotics and a brief hospital stay for hypoxia and confusion.
- During her stay allergy is consulted for clarification of her drug allergies
- She undergoes a graded dose challenge to penicillin
- Unfortunately, despite a successful challenge, the team forgets to delabel the penicillin allergy in the EMR





The Case for Clarifying Drug Allergies

- Benefits
 - First line therapy
 - Potentially lower cost
 - Patient safety
 - Drug drug interactions
- Timing
- · Deletion vs. clean up of duplicates
- · Labels with all parts
 - Specificity
 - Reaction vs. Unknown
 - Free text vs. codified



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?



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



Individual approach



- Talk to the patient
 - Ask about time frame, reaction details
- Remove duplicates
- Remove erroneous entries
- Address acute medication needs
- Tackle known entities: e.g. Penicillin
- Start with medications that have immune mediated reactions
- Help patient understand their list: smart phone, provider communication, safe lists



De-labelling success



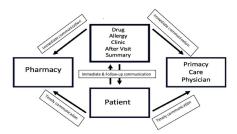
TABLE II. Drug allergy labels tested versus labels removed from EHR

Drug allergy labels tested	Attempted delabeling strategy	No. of labels tested	No. of labels removed from EHR
Penicillin	Skin testing* and oral challenge	393	390
Cephalosporins	Skin testing and oral challenge	209	201
Trimethoprim-sulfamethoxazole or sulfonamide	Single or graded oral challenge	177	167
Fluoroquinolones	Skin testing and oral challenge	97	93
NSAIDs	Graded oral challenge	27	25
Vancomycin	Historical	12	12
Radiocontrast	Skin testing	18	18
Azithromycin	Single or graded oral challenge	10	10

Vethody et al. Safety, Efficacy, and Effectiveness of Delabeling in Patients with Multiple Drug Allergy Labels. JACIP. Feb2021.

Interoperability





 $\textbf{FIGURE 2.} \ \ \textbf{Future interventions to improve effectiveness of care}$ in patients with MDALs.

Vethody et al. Safety, Efficacy, and Effectiveness of Delabeling in Patients with Multiple Drug Allergy Labels. JACIP. Feb2021.

NSAID, Nonsteroidal anti-inflammatory drug.

*Penicillin reagents used were penicillin G 1000 U/mL, penicillin G 10,000 U/mL, Pre pen (major determinant), minor determinant mixture, and amplicillin 25 mg/mL.

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

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)
- Do not skin test hemodynamically unstable patients
- Not all medications have skin testing
- State by state rules vary on requirement to oversee testing: allergists, pharmacists, RN, NP, trained MDs





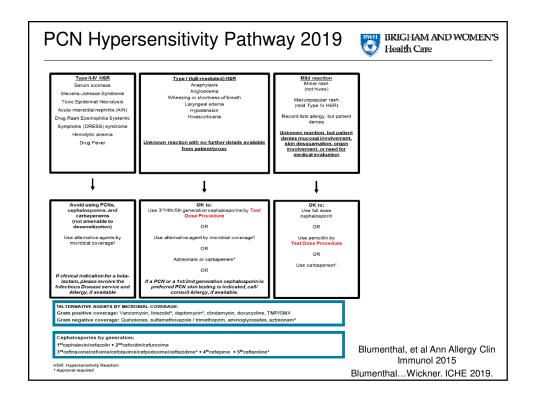


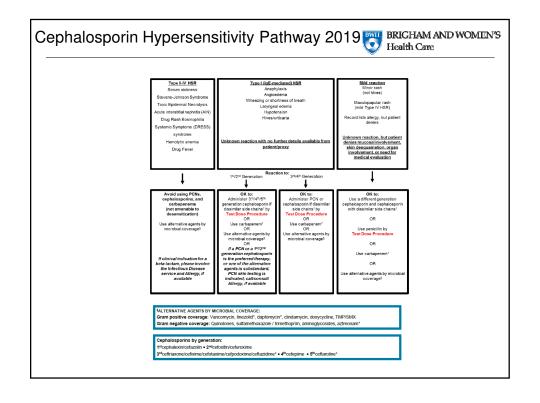
					SKIN TE	ST ORDE	R			
									ARN/PATIENT NAMI	E-DOB/DOS
Antibiotic	SPT	II)	ID				.19	ORIVIAITENI NAMI	EUDORIDOS
□ Azithromycin	100 mg/ml			0.01 mg/ml				-	To be seen by MD	prior to start of test
□ Aztreonam	3 mg/ml	0.3 mg		3 mg/ml				_	TO be seen by MID	prior to start or test
□ Cefazolin	330 mg/ml			33 mg/ml	Food: Entire	Ponel Lec	mmee: □ neanut	n souhean Tr	ree nuts: brazil nut	almond = necen
□ Cefotaxime	100 mg/ml			10 mg/ml	D cashew D engli	ch/black we	dnut a bazalnut	n pietachio n a	reen nea Crustassan s	hellfish: □ shrimp □ lobster □ crab
□ Ceftazidime	100 mg/ml			10 mg/ml	Molluscks (shell	fieh): m cla	n - oveter - cea	llon Fieh: - co	odfich = tuna = calmon	Dairy: - milk
□ Cetriaxone	100 mg/ml				Molluscks (shellfish): □ clam □ oystcr □ scallop Fish: □ codfish □ tuna □ salmon Dairy: □ milk □ cascin □ lactalbumin Grains: □ wheat □ rice □ oat □ barley □ rye Fruits: □ strawberry □ apple □ orange					
□ Cefuroxime	100 mg/ml			10 mg/ml					lery □ garlic □ onion o	
□ Ciprofloxacin	2 mg/ml	0.002 г		0.02 mg/ml	Meats: □ beef □ c				olk - baker's/brewer's	
□ Clindamycin	150 mg/ml			15 mg/ml		memen a p	от объ	minte D egg /c	one a bance abrever.	yease a sesame
□ Cotrimoxazole	80 mg/ml	0.08 m		0.8 mg/ml	Fresh Food:					
□ Erythromycin*	50 mg/ml	0.005 r	ng/ml	0.05 mg/ml						
□ Gentamicin	40 mg/ml	0.4 mg	/ml	4 mg/ml	Corticosteroid	SPT	ID	ID	ID	
□ Imipenem	1 mg/ml	0.1 mg		1 mg/ml	□ Prednisone	1mg/ml				
□ Levofloxacin	25 mg/ml	0.0025		0.025 mg/ml	□ Prednisolone	4mg/ml				
□ Moxifloxacin	1.6 mg/ml	/ 0.002 r		0.02 mg/ml	□ Depo-Medrol	40mg/ml	0.4mg/ml	4mg/ml		
□ Tobramycin	40 mg/ml	0.4 mg		4 mg/ml	□ Solumedrol	40mg/ml	0.4mg/ml	4mg/ml		
□ Vancomycin	50 mg/ml	0.0005		0.005 mg/ml	□ Decadron	4mg/ml	0.04 mg/ml	0.4mg/ml		
□ Ampicillin*	10 mg/ml	1 mg/m		10 mg/ml	□ Solue-Cortef		l 1mg/ml	10mg/ml		
□ Naficillin	250 mg/ml			0.025 mg/ml	□ Celestone	6mg/ml	0.6mg/ml	6mg/ml		
 Penicillin G 	10,000 u/m				□ Kenalog	10mg/ml	0.1 mg/ml	1 mg/ml	10mg/ml	
□ Pre Pen	undiluted	undilut								
□ Ticarcillin	200 mg/ml	2 mg/m	nl	20 mg/ml						
Chemotherapy	SPT	ID 7	m		Local Anesthetic					
□ Avastin*	25mg/ml	ID 0.25mg/ml	ID 2.5mg/m		Benzoic acid este	rs: Benz	ocaine Butacir	ie 🗆 Chlorproci	aine 2%/3% Cyclome	thycaine
□ Carboplatin	10mg/ml	1mg/ml .	10mg/ml		Office of P	rocaine 10	% □ Proparacaine	Opnthalmic 0.	.5% Propoxycaine	Tetracaine Ophthalmic 0.5%
□ Cisplatin	1mg/ml	0.1mg/ml	Img/ml		□ Lidocaine 0.5%.	Bupivac	ain 0.25%, 0.5%,	0.75% Dibt	ucaine 🗆 Dyclonine 🗆 E	tidocaine
□ Cytoxan	10mg/ml	lmg/ml	10mg/ml						ne, Prilocaine if negative 15 min. 1ml	P0.00
□ Oxaliplatin*	5mg/ml	0.5mg/ml	5mg/ml		Chanenge.		_ ii 51 negative, v	0.5 IIII F5 SC, 1	n negative 15 min. 1mi	F5 5C
□ Taxol*	1mg/ml	0.001mg/ml	0.01mg/m	1	General Anesthei	in	Prick	ID	ID	ID
	11116/1111	o.ooringiin	0.01mg/ii		Etomidate		2mg/ml	0.002 mg/m		0.2 mg/ml
					□ Fentanyl		50 ug/ml	0.002 mg/m		5ug/ml
Biologics	SPT	ID	ID	ID	□ Midazolam		5 mg/ml	0.005 ng/m		0.5 mg/ml
□ Abatacept*	25 mg/ml	0.025 mg/ml		ml 2.5 mg/ml	Pancuronium		2 mg/ml	0.003 mg/n		0.2 mg/ml
□ Copaxone	20 mg/ml	0.02 mg/ml	0.2 mg/m		□ Propofol		10 mg/ml	0.002 mg/ml		1 mg/ml
□ Etanecept	50 mg/ml	0.05/mg/ml	0.5 mg/m		□ Succinylcholine		20 mg/ml	0.001 mg/m		0.1 mg/ml
□ Infliximab*	10 mg/ml	0.1 mg/ml	1 mg/ml		□ Thiopental		25 mg/ml	0.025 mg/m		2.5 mg/ml
□ Methotrexate	25 mg/ml	0.25 mg/ml	2.5 mg/m	d	□ Vecuronium*		4 mg/ml	0.004 mg/m		0.4 mg/ml
□ Rebif	22mcg/ml	0.022mcg/ml		/ml 2.2 mcg/ml			9			
□ Rituximab*	10 mg/ml	0.01 mg/ml	0.1 mg/n	nl 1 mg/ml	□ Progesterone:	SP: Proge	sterone 50mg/ml	in Benzyl Alco	ohol and Benzyl Alcoho	l; ID 1/1000, 1/100, 1/10
□ Trastuzumab*	21 mg/ml	0.21 mg/ml	2.1 mg/m	d	☐ Ferrlecit*: SP:	12.5 mg/m	l; ID: 0.0125 mg	/ml, 0.125 mg/	ml, 1.25 mg/ml(DO NO	T TEST TO VENOFER)
Insulin: SP undiluted, ID: 1:1000, 1:100 and 1:10 □ Apidra □ Humalog □ Humulin N □ Humulin N										
Venom: □ Entire Panel □ Honey Bee □ Wasp □ Lantus □ Levemir □ Novolin N □ Sterile diluent										
□ White Faced Hornet □ Yellow Hornet □ Yellow Jacket										
□ <u>Other:</u>										
Environmental:	□ Entire SP	T Panel, ID TBI	after SPT				Ordering MD:			MD Initials:
Environmental: □ Entire SPT Panel, ID TBD after SPT □ Dust □ Cat □ Alternaria □ Penicillium □ Dog □ Cockroach □ Oak □ Grass □ Hormodendrum □ Dust □ Cat □ Alternaria □ Penicillium □ Dog □ Cockroach □ Oak □ Grass □ Hormodendrum										
□ Ragweed □ Grass □ Feather □ Brich □ Plantain □ □ BWH Weed □ BWH Tree □ Mugwort □ Aspergillus □ Other: □ □ Mouse □ Rat □ *PM testing only due to stability of medication										
□ Aspergillus □ Other: □ □ Mouse □ Rat □ *PM testing only due to stability of medication										

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 w/ PCN allergy



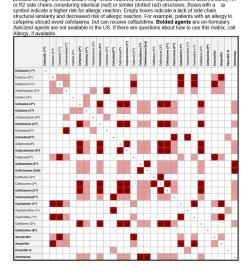
- Not straightforward- if you have an allergy consult service, utilize it
- Macy et al April 2021 JAMA Network- removed cross reactivity warning in PCN allergic patients >4million studied, no safety issues identified, increased cephalosporin use
- For patients with mild cutaneous reactions without features of an IgE reaction UpToDate recommends:
 - Usually ok to give 3rd/4th/5th generation cephalosporin
 - Ok to give a carbapenem

Blumenthal K & Solensky R. Choice of antibiotics in penicillin-allergic hospitalized patients.UpToDate. Accessed on Sept 2022

- Ok to give aztreonam
- Give 1st/2nd generation cephalosporins or penicillins via test dose

Cephalosporin cross reactivity

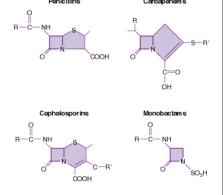




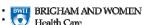
Aztreonam



- · 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



When to call allergy (if available): We BRICHAM 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

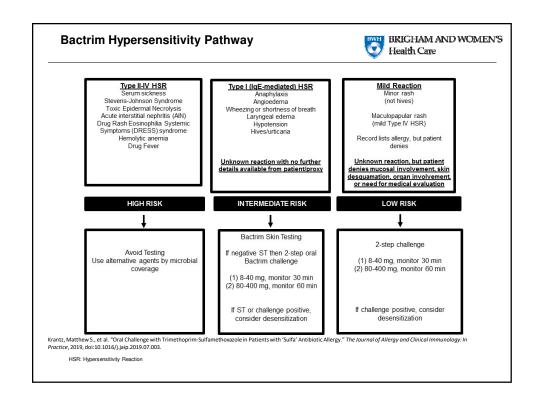
What if there is no allergy to call! BRIGHAM AND WOMEN'S Health Care



- · 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



BRICHAM AND WOMEN'S Outline Health Care Drug allergies Oxycodone Penicillins **Basics** Ι. SWELLING Beta lactam Sugar-protein-starch Pt reports she "craves" for more of the sugar and starch (flour) III. Sulfa IV. Fluoroquinolones V. Contrast allergy II. Immunodeficiency III. Anaphylaxis



Sulfa allergy



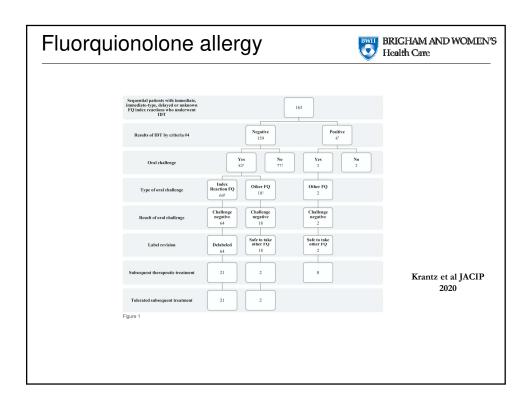
For patients with morbilliform rash without fever or other severe cutaneous symptoms (SJS etc) can be done as outpatient or inpatient and does not require ICU

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			

Fluoroquinolones



- Most frequently reported non beta lactam antibiotic allergy
- Cross reactivity not complete between fluoroquionolones, allergists can often challenge to clarify safety of alternative FQ use
- · Skin testing of questionable utility



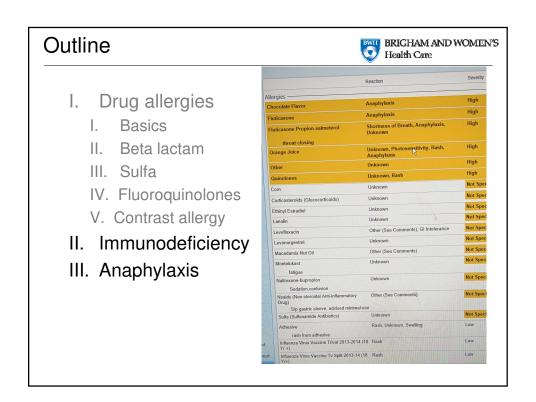
Contrast allergy: myth and pearls

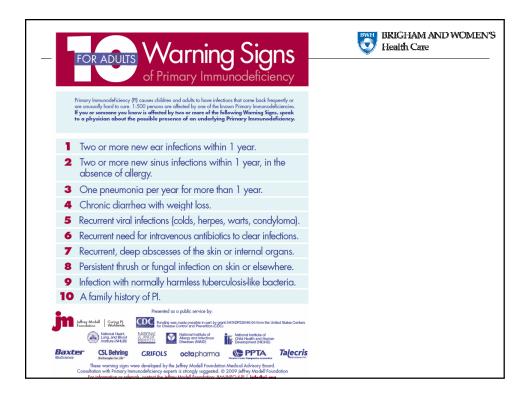




- Primary prevention usually not necessary
- NO CORRELATION WITH SHELLFISH, IODIDE
- Testing not widely used in US
- Premedication works well.

- Greenberger protocol:
 - 50mg prednisone 13,7, 1 hour prior
 - 10mg cetirizine (or 50mg benadryl IV) 1 hour before





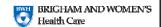
Immunodeficiency: CVID



Diagnosis: at least two of immunoglobulin isotypes 2 SD below the mean for age values (usually IgG and IgA+/-M) AND all of the following:

- a. >2years of age
- b. poor response to vaccination (protein and polysaccharide)
- c. other defined causes of hypogammaglobulinemia have been excluded

Immunodeficiency: CVID



Immunodeficiency doesn't always present with recurrent infections

<u>Autoimmune disease</u> (ex. autoimmune hemolytic anemia or thrombocytopenia in CVID, SLE-like syndrome in complement def.)

Unusual <u>lymphoid and granulomatous diseases</u> (ex. Sarcoid-like lung disease in patients with CVID)

Malignancies

Vaccine responses: pre and post vaccination

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Streptococcus pneumoniae Antibodies, IgG (14 serotypes)
     PNEUMOCOCCAL SEROTYPE 1, IgG 0.03 ug/mL
PNEUMOCOCCAL SEROTYPE 3, IgG 0.01 ug/mL
                                                                              0.05 ug/mL
                                                           0.01 ug/mL
                                                                              0.11 ug/mL
     PNEUMOCOCCAL SEROTYPE 4*, IgG
PNEUMOCOCCAL SEROTYPE 5, IgG
                                                           0.01 ug/mL
                                                                              0.01 ug/mL
                                                           0.03 ug/mL
                                                                              0.03 ug/mL
     PNEUMOCOCCAL SEROTYPE 6B*, IgG
                                                           0.08 ug/mL
                                                                              0.05 ug/mL
     PNEUMOCCOCAL SEROTYPE 7F, IgG
                                                           0.04 ug/mL
                                                                             0.27 ug/mL
     PNEUMOCOCCAL SEROTYPE 8, IgG
PNEUMOCOCCAL SEROTYPE 9N, IgG
                                                           0.10 ug/mL
                                                                             0.06 ug/mL
                                                           0.01 ug/mL
                                                                             0.02 ug/mL
     PNEUMOCOCCAL SEROTYPE 9V*, IgG
                                                           0.04 ug/mL
                                                                             0.07 ug/mL
     PNEUMOCOCCAL SEROTYPE 12F, IgG
PNEUMOCOCCAL SEROTYPE 14*, IgG
                                                           0.03 ug/mL
                                                                             0.03 ug/mL
                                                           0.02 ug/mL
                                                                             0.04 ug/mL
     PNEUMOCOCCAL SERCTYPE 18C*, IgG
PNEUMOCOCCAL SERCTYPE 19F*, IgG
PNEUMOCOCCAL SERCTYPE 23F*, IgG
                                                           0.02 ug/mL
                                                                             0.02 ug/mL
                                                           0.05 ug/mL
                                                                             0.04 ug/mL
                                                           0.01 ug/mL
                                                                             0.01 ug/mL
     PNEUMO SEROTYPE INTERPRETATION
                                                           SEE NOTE
                                                                             SEE NOTE
         INTERPRETATION: Pneumococcal Antibodies, IgG
Includes serotypes 1, 3, 4*, 5, 6B*, 7F, 8, 9N, 9V*, 12F, 14*, 18C*, 19F*, 23F*
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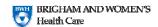
BRIGHAM AND WOMEN'S Health Care My unvaccinated titers: twins in daycare S. pneumoniae IgG Ab, 23 serotypes, S Serotype 1 (1) mcg/mL Serotype 2(2) 6.8 mcg/mL Serotype 3 (3) 17.1 mcg/mL Serotype 4 (4) 4.9 mcg/mL Serotype 5 (5) 31.5 mcg/mL Serotype 8 (8) 12.0 mcg/mL Serotype 9N (9) Serotype 12F (12) 27.4 mcg/mL 6.9 mcg/mL Serotype 14 (14) Serotype 17F (17) 19.7 mcq/mL 85.6 mcg/mL Serotype 19F (19) 54.2 mcg/mL Serotype 20 (20) 11.1 mcg/mL Serotype 22F (22) 122.8 mcg/mL Serotype 23F (23) 102.2 mcg/mL Serotype 6B (26) 27.6 Serotype 10A (34) mcg/mL 59.6 mcg/mL Serotype 11A (43) 5.8 mcg/mL Serotype 7F (51) 69.3 mcg/mL Serotype 15B (54) 19.8 mcg/mL Serotype 18C (56) 2.8 mcg/mL Serotype 19A (57) 25.6 mcg/mL Serotype 9V (68) 31.2 mcg/mL Serotype 33F (70) mcg/mL

CASE 2: Anaphylaxis



- 20 yo male with peanut allergy admitted for nephrolithiasis
- Day 2 of his admission he takes a bite of a pad thai noodle dish brought in by a friend.
 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?

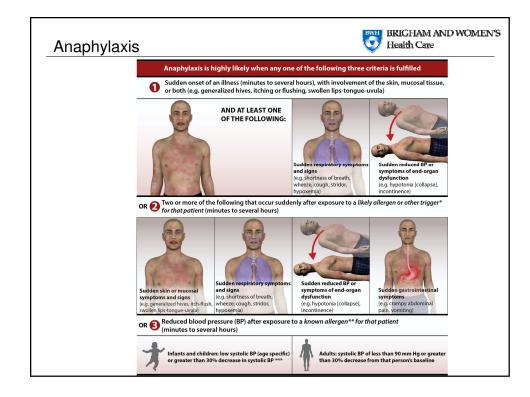


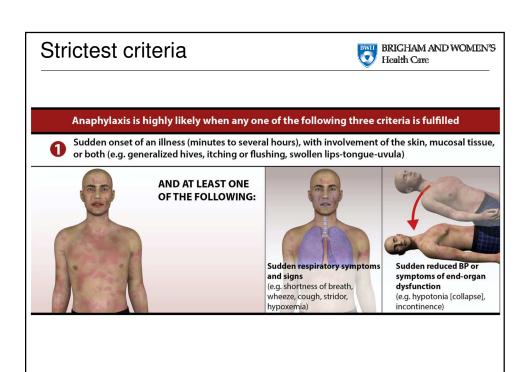
Here's my advice.....

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

TO DO LIST

Follow Op Follow Op . . .

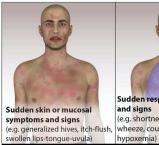


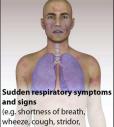


Likely exposure criteria



OR 2 Two or more of the following that occur suddenly after exposure to a *likely allergen or other trigger** for that patient (minutes to several hours)











pain, vomiting)

Exposure to patient known allergen



OR 8 Reduced blood pressure (BP) after exposure to a known allergen** for that patient (minutes to several hours)





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 2: follow up



- Given Epi IM x1, cetirzine, and solumedrol.
- Monitored vital signs and symptoms x 2 hours
- Reviewed epinephrine use and carrying portable epinephrine, asking and reading labels
- Reviewed ingredients of noodle dish, contained peanut

Case 2: follow up



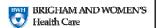
- · Seek emergency care
- · Follow up for testing
- List allergy in allergy section of medical record and communicate to patient (smart phone etc)
- Does not need epipen prescription

Case 4: High risk



- A patient in your practice has repeated urinary tract infections requiring IV antibiotics.
- You sent them to allergy 5 years ago, where her TMP/SMX and PCN allergies were cleared
- She is on a repeat course of antibiotics and develops hives

Conclusions



- Know what questions to ask to clarify drug allergies
- Understand complexities of penicillin and cephalosporin allergies
- · Review sulfa and other antibiotic allergies
- When to call/refer to an allergist
- Partnership in cleaning up the EMR allergy section
- Anaphylaxis 101
- The porpoise....