

Allergy 101: Drug Allergy and Other common Consults for Hospitalists

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Disclosures

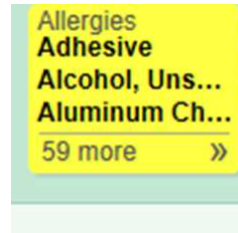


- Dual employment, VP of Enterprise Patient Safety at CVS Health. Nothing discussed today relevant to role at CVS Health

Outline

I. Drug allergies

- I. Basics
- II. Beta lactam
- III. Sulfa
- IV. Fluoroquinolones
- V. Contrast allergy



II. Immunodeficiency

III. Anaphylaxis



= New 2024 Content

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 de-label 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

- 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

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 ampicillin 25 mg/mL.

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

Interoperability

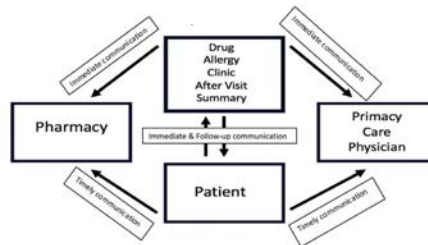


FIGURE 2. Future interventions to improve effectiveness of care in patients with MDALs.

Vethody et al. Safety, Efficacy, and Effectiveness of Delabeling in Patients with Multiple Drug Allergy Labels. JACIP. Feb 2021.

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, GBS in pregnancy
- 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, not everyone needs a skin test prior to a challenge
- State by state rules vary on requirement to oversee testing: allergists, pharmacists, RN, NP, trained MDs



SKIN TEST ORDER				MRN/PATIENT NAME/DOB/DO			
Antibiotic <input type="checkbox"/> Azithromycin 100 mg/ml SPT ID ID <input type="checkbox"/> Aztreonam 3 mg/ml 0.001 mg/ml 0.01 mg/ml <input type="checkbox"/> Cefazolin 330 mg/ml 3 mg/ml 3 mg/ml <input type="checkbox"/> Cefazoxime 100 mg/ml 1 mg/ml 10 mg/ml <input type="checkbox"/> Ceftriaxone 100 mg/ml 1 mg/ml 10 mg/ml <input type="checkbox"/> Cefuroxime 100 mg/ml 1 mg/ml 10 mg/ml <input type="checkbox"/> Ciprofloxacin 2 mg/ml 0.002 mg/ml 0.02 mg/ml <input type="checkbox"/> Clindamycin 150 mg/ml 1.5 mg/ml 15 mg/ml <input type="checkbox"/> Cotrimoxazole 80 mg/ml 0.08 mg/ml 0.8 mg/ml <input type="checkbox"/> Erythromycin* 50 mg/ml 0.005 mg/ml 0.05 mg/ml <input type="checkbox"/> Gentamicin 40 mg/ml 0.4 mg/ml 4 mg/ml <input type="checkbox"/> Imipenem 1 mg/ml 0.1 mg/ml 1 mg/ml <input type="checkbox"/> Levofloxacin 25 mg/ml 0.0025 mg/ml 0.025 mg/ml <input type="checkbox"/> Moxifloxacin 1.6 mg/ml 0.002 mg/ml 0.02 mg/ml <input type="checkbox"/> Tobramycin 40 mg/ml 0.4 mg/ml 4 mg/ml <input type="checkbox"/> Vancomycin 50 mg/ml 0.0005 mg/ml 0.005 mg/ml <input type="checkbox"/> Ampicillin* 10 mg/ml 1 mg/ml 10 mg/ml <input type="checkbox"/> Nafcillin 250 mg/ml 0.0025 mg/ml 0.025 mg/ml <input type="checkbox"/> Penicillin G 10,000 u/ml 10,000 u/ml <input type="checkbox"/> Pre Pen undiluted <input type="checkbox"/> Ticarcillin 200 mg/ml 2 mg/ml 20 mg/ml				Food: <input type="checkbox"/> Entire Panel <input type="checkbox"/> Legumes: <input type="checkbox"/> peanut <input type="checkbox"/> soybean <input type="checkbox"/> Tree nuts: <input type="checkbox"/> brazil nut <input type="checkbox"/> almond <input type="checkbox"/> pecan <input type="checkbox"/> cashew <input type="checkbox"/> english/black walnut <input type="checkbox"/> hazelnut <input type="checkbox"/> pistachio <input type="checkbox"/> green pea <input type="checkbox"/> Crustacean shellfish: <input type="checkbox"/> shrimp <input type="checkbox"/> lobster <input type="checkbox"/> crab <input type="checkbox"/> Mollusks (shellfish): <input type="checkbox"/> clam <input type="checkbox"/> oyster <input type="checkbox"/> scallop <input type="checkbox"/> Fish: <input type="checkbox"/> codfish <input type="checkbox"/> tuna <input type="checkbox"/> salmon <input type="checkbox"/> Dairy: <input type="checkbox"/> milk <input type="checkbox"/> casein <input type="checkbox"/> lactalbumin <input type="checkbox"/> Grains: <input type="checkbox"/> wheat <input type="checkbox"/> rice <input type="checkbox"/> oat <input type="checkbox"/> barley <input type="checkbox"/> rye <input type="checkbox"/> Fruits: <input type="checkbox"/> strawberry <input type="checkbox"/> apple <input type="checkbox"/> orange Vegetables: <input type="checkbox"/> corn <input type="checkbox"/> tomato <input type="checkbox"/> white potato <input type="checkbox"/> carrot <input type="checkbox"/> celery <input type="checkbox"/> garlic <input type="checkbox"/> onion <input type="checkbox"/> ginger Meats: <input type="checkbox"/> beef <input type="checkbox"/> chicken <input type="checkbox"/> pork <input type="checkbox"/> egg white <input type="checkbox"/> egg yolk <input type="checkbox"/> baker's/brewer's yeast <input type="checkbox"/> sesame			
Chemotherapy <input type="checkbox"/> Avastin* 25mg/ml SPT ID ID <input type="checkbox"/> Carboplatin 10mg/ml 1mg/ml 10mg/ml <input type="checkbox"/> Cisplatin 1mg/ml 0.1mg/ml 1mg/ml <input type="checkbox"/> Cytosin 10mg/ml 1mg/ml 10mg/ml <input type="checkbox"/> Oxaliplatin* 5mg/ml 0.5mg/ml 5mg/ml <input type="checkbox"/> Taxol* 1mg/ml 0.001mg/ml 0.01mg/ml				Local Anesthetic: Prick FS, ID 1/100, 1/10, FS Benzocaine acid esters: <input type="checkbox"/> Benzocaine <input type="checkbox"/> Butacaine <input type="checkbox"/> Chlorprocaine 2%/3% <input type="checkbox"/> Cyclomethycaine <input type="checkbox"/> Hexylcaine <input type="checkbox"/> Procaine 10% <input type="checkbox"/> Proparacaine Ophthalmic 0.5% <input type="checkbox"/> Propoxycaine <input type="checkbox"/> Tetracaine Ophthalmic 0.5% Other (Amides): <input type="checkbox"/> Bupivacaine 0.25%, 0.5%, 0.75% <input type="checkbox"/> Dibucaine <input type="checkbox"/> Dyclonine <input type="checkbox"/> Etidocaine <input type="checkbox"/> Lidocaine 0.5%, 1%, 2% <input type="checkbox"/> Mepivacaine 1%, 2%, 3% <input type="checkbox"/> Prilocaine Challenge: _____ if ST negative, 0.3 ml FS SC, if negative 15 min. 1ml FS SC			
Biologics <input type="checkbox"/> Abatacept* 25 mg/ml SPT ID ID ID <input type="checkbox"/> Copaxone 20 mg/ml 0.025 mg/ml 0.25 mg/ml 2.5 mg/ml <input type="checkbox"/> Etanercept 50 mg/ml 0.05 mg/ml 0.5 mg/ml 5mg/ml <input type="checkbox"/> Infliximab* 1mg/ml 0.1 mg/ml 1mg/ml -- <input type="checkbox"/> Methotrexate 25 mg/ml 0.25 mg/ml 2.5 mg/ml -- <input type="checkbox"/> Rebif 22mcg/ml 0.022mcg/ml 0.22 mcg/ml 2.2 mcg/ml <input type="checkbox"/> Rituximab* 10 mg/ml 0.01 mg/ml 0.1 mg/ml 1 mg/ml <input type="checkbox"/> Trastuzumab* 21 mg/ml 0.21 mg/ml 2.1 mg/ml --				General Anesthetics: <input type="checkbox"/> Etomidate 2mg/ml SPT ID ID ID <input type="checkbox"/> Fentanyl 50 ug/ml 0.002 mg/ml 0.02 mg/ml 0.2 mg/ml <input type="checkbox"/> Midazolam 5 mg/ml 0.005 mg/ml 0.05 mg/ml 0.5 mg/ml <input type="checkbox"/> Pancuronium 2 mg/ml 0.002 mg/ml 0.02 mg/ml 0.2 mg/ml <input type="checkbox"/> Propofol 10 mg/ml 0.01 mg/ml 0.1 mg/ml 1 mg/ml <input type="checkbox"/> Succinylcholine 20 mg/ml 0.001 mg/ml 0.01 mg/ml 0.1 mg/ml <input type="checkbox"/> Thiopental 25 mg/ml 0.025 mg/ml 0.25 mg/ml 2.5 mg/ml <input type="checkbox"/> Vecuronium* 4 mg/ml 0.004 mg/ml 0.04 mg/ml 0.4 mg/ml			
Venoms: <input type="checkbox"/> Entire Panel <input type="checkbox"/> Honey Bee <input type="checkbox"/> Wasp <input type="checkbox"/> White Faced Hornet <input type="checkbox"/> Yellow Hornet <input type="checkbox"/> Yellow Jacket				Other: <input type="checkbox"/> Entire SPT Panel, ID TBD after SPT <input type="checkbox"/> Dust <input type="checkbox"/> Cat <input type="checkbox"/> Alternaria <input type="checkbox"/> Penicillium <input type="checkbox"/> Dog <input type="checkbox"/> Cockroach <input type="checkbox"/> Oak <input type="checkbox"/> Grass <input type="checkbox"/> Hormodendrum <input type="checkbox"/> Ragweed <input type="checkbox"/> Grass <input type="checkbox"/> Feather <input type="checkbox"/> Birch <input type="checkbox"/> Plantain <input type="checkbox"/> BWH Weed <input type="checkbox"/> BWH Tree <input type="checkbox"/> Mugwort <input type="checkbox"/> Aspergillus <input type="checkbox"/> Other: _____ <input type="checkbox"/> Mouse <input type="checkbox"/> Rat			
Ordering MD: _____ MD Initials: _____ Date: _____ Time: _____ * 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?

Tools for Penicillin Allergy



- PEN-FAST tool to score allergy risk in adults
 - F: Five years or less since reaction (2pts)
 - A: Anaphylaxis/angioedema or
 - S: Severe cutaneous adverse reaction (2 points)
 - T: Treatment required (1 point)

Total score of 2 or lower able to tolerate PCN 100% NPV. For low scores, single or graded dose challenge with 500mg amoxicillin with observation period.

Other tools and studies (Macy et al) to risk stratify PCN allergic patients.



Su C et al. JAMA Intern Med 2023
Trubiano et al. JAMA Intern Med 2020

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
 - 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 2023

Cephalosporin cross reactivity



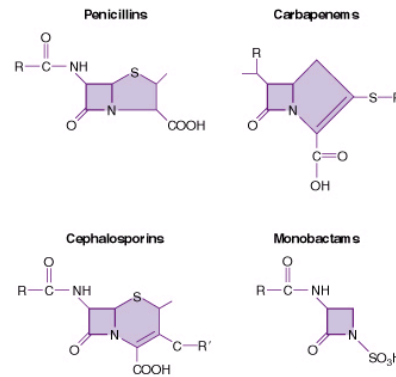
Cross-Reactivity Among Cephalosporins

This matrix is intended for use with the penicillin and cephalosporin allergy pathways. This matrix describes cross-reactivity risk for patients considering side chain structure. Cross-reactivity is also possible through the beta-lactam ring. Cross-reactivity between cephalosporins is determined by R1 or R2 side chains considering identical (red) or similar (dotted red) structures. Boxes with a ⊕ symbol indicate a higher risk for allergic reaction. Empty boxes indicate a lack of side chain structural similarity and decreased risk of allergic reaction. For example, patients with an allergy to cefepime should avoid cefotaxime, but can receive ceftazidime. **Bolded agents** are on-formulary. *Italicized agents* are not available in the US. If there are questions about how to use this matrix, call Allergy, if available.

Antibiotic	Cefazolin (1 st)	Cefazolin (2 nd)	Cefazolin (3 rd)	Cefazolin (4 th)	Cefazolin (5 th)	Cefazolin (6 th)	Cefazolin (7 th)	Cefazolin (8 th)	Cefazolin (9 th)	Cefazolin (10 th)	Cefazolin (11 th)	Cefazolin (12 th)	Cefazolin (13 th)	Cefazolin (14 th)	Cefazolin (15 th)	Cefazolin (16 th)	Cefazolin (17 th)	Cefazolin (18 th)	Cefazolin (19 th)	Cefazolin (20 th)	Cefazolin (21 st)	Cefazolin (22 nd)	Cefazolin (23 rd)	Cefazolin (24 th)	Cefazolin (25 th)	Cefazolin (26 th)	Cefazolin (27 th)	Cefazolin (28 th)	Cefazolin (29 th)	Cefazolin (30 th)	Cefazolin (31 st)	Cefazolin (32 nd)	Cefazolin (33 rd)	Cefazolin (34 th)	Cefazolin (35 th)	Cefazolin (36 th)	Cefazolin (37 th)	Cefazolin (38 th)	Cefazolin (39 th)	Cefazolin (40 th)	Cefazolin (41 st)	Cefazolin (42 nd)	Cefazolin (43 rd)	Cefazolin (44 th)	Cefazolin (45 th)	Cefazolin (46 th)	Cefazolin (47 th)	Cefazolin (48 th)	Cefazolin (49 th)	Cefazolin (50 th)	Cefazolin (51 st)	Cefazolin (52 nd)	Cefazolin (53 rd)	Cefazolin (54 th)	Cefazolin (55 th)	Cefazolin (56 th)	Cefazolin (57 th)	Cefazolin (58 th)	Cefazolin (59 th)	Cefazolin (60 th)	Cefazolin (61 st)	Cefazolin (62 nd)	Cefazolin (63 rd)	Cefazolin (64 th)	Cefazolin (65 th)	Cefazolin (66 th)	Cefazolin (67 th)	Cefazolin (68 th)	Cefazolin (69 th)	Cefazolin (70 th)	Cefazolin (71 st)	Cefazolin (72 nd)	Cefazolin (73 rd)	Cefazolin (74 th)	Cefazolin (75 th)	Cefazolin (76 th)	Cefazolin (77 th)	Cefazolin (78 th)	Cefazolin (79 th)	Cefazolin (80 th)	Cefazolin (81 st)	Cefazolin (82 nd)	Cefazolin (83 rd)	Cefazolin (84 th)	Cefazolin (85 th)	Cefazolin (86 th)	Cefazolin (87 th)	Cefazolin (88 th)	Cefazolin (89 th)	Cefazolin (90 th)	Cefazolin (91 st)	Cefazolin (92 nd)	Cefazolin (93 rd)	Cefazolin (94 th)	Cefazolin (95 th)	Cefazolin (96 th)	Cefazolin (97 th)	Cefazolin (98 th)	Cefazolin (99 th)	Cefazolin (100 th)	Cefazolin (101 st)	Cefazolin (102 nd)	Cefazolin (103 rd)	Cefazolin (104 th)	Cefazolin (105 th)	Cefazolin (106 th)	Cefazolin (107 th)	Cefazolin (108 th)	Cefazolin (109 th)	Cefazolin (110 th)	Cefazolin (111 st)	Cefazolin (112 nd)	Cefazolin (113 rd)	Cefazolin (114 th)	Cefazolin (115 th)	Cefazolin (116 th)	Cefazolin (117 th)	Cefazolin (118 th)	Cefazolin (119 th)	Cefazolin (120 th)	Cefazolin (121 st)	Cefazolin (122 nd)	Cefazolin (123 rd)	Cefazolin (124 th)	Cefazolin (125 th)	Cefazolin (126 th)	Cefazolin (127 th)	Cefazolin (128 th)	Cefazolin (129 th)	Cefazolin (130 th)	Cefazolin (131 st)	Cefazolin (132 nd)	Cefazolin (133 rd)	Cefazolin (134 th)	Cefazolin (135 th)	Cefazolin (136 th)	Cefazolin (137 th)	Cefazolin (138 th)	Cefazolin (139 th)	Cefazolin (140 th)	Cefazolin (141 st)	Cefazolin (142 nd)	Cefazolin (143 rd)	Cefazolin (144 th)	Cefazolin (145 th)	Cefazolin (146 th)	Cefazolin (147 th)	Cefazolin (148 th)	Cefazolin (149 th)	Cefazolin (150 th)	Cefazolin (151 st)	Cefazolin (152 nd)	Cefazolin (153 rd)	Cefazolin (154 th)	Cefazolin (155 th)	Cefazolin (156 th)	Cefazolin (157 th)	Cefazolin (158 th)	Cefazolin (159 th)	Cefazolin (160 th)	Cefazolin (161 st)	Cefazolin (162 nd)	Cefazolin (163 rd)	Cefazolin (164 th)	Cefazolin (165 th)	Cefazolin (166 th)	Cefazolin (167 th)	Cefazolin (168 th)	Cefazolin (169 th)	Cefazolin (170 th)	Cefazolin (171 st)	Cefazolin (172 nd)	Cefazolin (173 rd)	Cefazolin (174 th)	Cefazolin (175 th)	Cefazolin (176 th)	Cefazolin (177 th)	Cefazolin (178 th)	Cefazolin (179 th)	Cefazolin (180 th)	Cefazolin (181 st)	Cefazolin (182 nd)	Cefazolin (183 rd)	Cefazolin (184 th)	Cefazolin (185 th)	Cefazolin (186 th)	Cefazolin (187 th)	Cefazolin (188 th)	Cefazolin (189 th)	Cefazolin (190 th)	Cefazolin (191 st)	Cefazolin (192 nd)	Cefazolin (193 rd)	Cefazolin (194 th)	Cefazolin (195 th)	Cefazolin (196 th)	Cefazolin (197 th)	Cefazolin (198 th)	Cefazolin (199 th)	Cefazolin (200 th)	Cefazolin (201 st)	Cefazolin (202 nd)	Cefazolin (203 rd)	Cefazolin (204 th)	Cefazolin (205 th)	Cefazolin (206 th)	Cefazolin (207 th)	Cefazolin (208 th)	Cefazolin (209 th)	Cefazolin (210 th)	Cefazolin (211 st)	Cefazolin (212 nd)	Cefazolin (213 rd)	Cefazolin (214 th)	Cefazolin (215 th)	Cefazolin (216 th)	Cefazolin (217 th)	Cefazolin (218 th)	Cefazolin (219 th)	Cefazolin (220 th)	Cefazolin (221 st)	Cefazolin (222 nd)	Cefazolin (223 rd)	Cefazolin (224 th)	Cefazolin (225 th)	Cefazolin (226 th)	Cefazolin (227 th)	Cefazolin (228 th)	Cefazolin (229 th)	Cefazolin (230 th)	Cefazolin (231 st)	Cefazolin (232 nd)	Cefazolin (233 rd)	Cefazolin (234 th)	Cefazolin (235 th)	Cefazolin (236 th)	Cefazolin (237 th)	Cefazolin (238 th)	Cefazolin (239 th)	Cefazolin (240 th)	Cefazolin (241 st)	Cefazolin (242 nd)	Cefazolin (243 rd)	Cefazolin (244 th)	Cefazolin (245 th)	Cefazolin (246 th)	Cefazolin (247 th)	Cefazolin (248 th)	Cefazolin (249 th)	Cefazolin (250 th)	Cefazolin (251 st)	Cefazolin (252 nd)	Cefazolin (253 rd)	Cefazolin (254 th)	Cefazolin (255 th)	Cefazolin (256 th)	Cefazolin (257 th)	Cefazolin (258 th)	Cefazolin (259 th)	Cefazolin (260 th)	Cefazolin (261 st)	Cefazolin (262 nd)	Cefazolin (263 rd)	Cefazolin (264 th)	Cefazolin (265 th)	Cefazolin (266 th)	Cefazolin (267 th)	Cefazolin (268 th)	Cefazolin (269 th)	Cefazolin (270 th)	Cefazolin (271 st)	Cefazolin (272 nd)	Cefazolin (273 rd)	Cefazolin (274 th)	Cefazolin (275 th)	Cefazolin (276 th)	Cefazolin (277 th)	Cefazolin (278 th)	Cefazolin (279 th)	Cefazolin (280 th)	Cefazolin (281 st)	Cefazolin (282 nd)	Cefazolin (283 rd)	Cefazolin (284 th)	Cefazolin (285 th)	Cefazolin (286 th)	Cefazolin (287 th)	Cefazolin (288 th)	Cefazolin (289 th)	Cefazolin (290 th)	Cefazolin (291 st)	Cefazolin (292 nd)	Cefazolin (293 rd)	Cefazolin (294 th)	Cefazolin (295 th)	Cefazolin (296 th)	Cefazolin (297 th)	Cefazolin (298 th)	Cefazolin (299 th)	Cefazolin (300 th)	Cefazolin (301 st)	Cefazolin (302 nd)	Cefazolin (303 rd)	Cefazolin (304 th)	Cefazolin (305 th)	Cefazolin (306 th)	Cefazolin (307 th)	Cefazolin (308 th)	Cefazolin (309 th)	Cefazolin (310 th)	Cefazolin (311 st)	Cefazolin (312 nd)	Cefazolin (313 rd)	Cefazolin (314 th)	Cefazolin (315 th)	Cefazolin (316 th)	Cefazolin (317 th)	Cefazolin (318 th)	Cefazolin (319 th)	Cefazolin (320 th)	Cefazolin (321 st)	Cefazolin (322 nd)	Cefazolin (323 rd)	Cefazolin (324 th)	Cefazolin (325 th)	Cefazolin (326 th)	Cefazolin (327 th)	Cefazolin (328 th)	Cefazolin (329 th)	Cefazolin (330 th)	Cefazolin (331 st)	Cefazolin (332 nd)	Cefazolin (333 rd)	Cefazolin (334 th)	Cefazolin (335 th)	Cefazolin (336 th)	Cefazolin (337 th)	Cefazolin (338 th)	Cefazolin (339 th)	Cefazolin (340 th)	Cefazolin (341 st)	Cefazolin (342 nd)	Cefazolin (343 rd)	Cefazolin (344 th)	Cefazolin (345 th)	Cefazolin (346 th)	Cefazolin (347 th)	Cefazolin (348 th)	Cefazolin (349 th)	Cefazolin (350 th)	Cefazolin (351 st)	Cefazolin (352 nd)	Cefazolin (353 rd)	Cefazolin (354 th)	Cefazolin (355 th)	Cefazolin (356 th)	Cefazolin (357 th)	Cefazolin (358 th)	Cefazolin (359 th)	Cefazolin (360 th)	Cefazolin (361 st)	Cefazolin (362 nd)	Cefazolin (363 rd)	Cefazolin (364 th)	Cefazolin (365 th)	Cefazolin (366 th)	Cefazolin (367 th)	Cefazolin (368 th)	Cefazolin (369 th)	Cefazolin (370 th)	Cefazolin (371 st)	Cefazolin (372 nd)	Cefazolin (373 rd)	Cefazolin (374 th)	Cefazolin (375 th)	Cefazolin (376 th)	Cefazolin (377 th)	Cefazolin (378 th)	Cefazolin (379 th)	Cefazolin (380 th)	Cefazolin (381 st)	Cefazolin (382 nd)	Cefazolin (383 rd)	Cefazolin (384 th)	Cefazolin (385 th)	Cefazolin (386 th)	Cefazolin (387 th)	Cefazolin (388 th)	Cefazolin (389 th)	Cefazolin (390 th)	Cefazolin (391 st)	Cefazolin (392 nd)	Cefazolin (393 rd)	Cefazolin (394 th)	Cefazolin (395 th)	Cefazolin (396 th)	Cefazolin (397 th)	Cefazolin (398 th)	Cefazolin (399 th)	Cefazolin (400 th)	Cefazolin (401 st)	Cefazolin (402 nd)	Cefazolin (403 rd)	Cefazolin (404 th)	Cefazolin (405 th)	Cefazolin (406 th)	Cefazolin (407 th)	Cefazolin (408 th)	Cefazolin (409 th)	Cefazolin (410 th)	Cefazolin (411 st)	Cefazolin (412 nd)	Cefazolin (413 rd)	Cefazolin (414 th)	Cefazolin (415 th)	Cefazolin (416 th)	Cefazolin (417 th)	Cefazolin (418 th)	Cefazolin (419 th)	Cefazolin (420 th)	Cefazolin (421 st)	Cefazolin (422 nd)	Cefazolin (423 rd)	Cefazolin (424 th)	Cefazolin (425 th)	Cefazolin (426 th)	Cefazolin (427 th)	Cefazolin (428 th)	Cefazolin (429 th)	Cefazolin (430 th)	Cefazolin (431 st)	Cefazolin (432 nd)	Cefazolin (433 rd)	Cefazolin (434 th)	Cefazolin (435 th)	Cefazolin (436 th)	Cefazolin (437 th)	Cefazolin (438 th)	Cefazolin (439 th)	Cefazolin (440 th)	Cefazolin (441 st)	Cefazolin (442 nd)	Cefazolin (443 rd)	Cefazolin (444 th)	Cefazolin (445 th)	Cefazolin (446 th)	Cefazolin (447 th)	Cefazolin (448 th)	Cefazolin (449 th)	Cefazolin (450 th)	Cefazolin (451 st)	Cefazolin (452 nd)	Cefazolin (453 rd)	Cefazolin (454 th)	Cefazolin (455 th)	Cefazolin (456 th)	Cefazolin (457 th)	Cefazolin (458 th)	Cefazolin (459 th)	Cefazolin (460 th)	Cefazolin (461 st)	Cefazolin (462 nd)	Cefazolin (463 rd)	Cefazolin (464 th)	Cefazolin (465 th)	Cefazolin (466 th)	Cefazolin (467 th)	Cefazolin (468 th)	Cefazolin (469 th)	Cefazolin (470 th)	Cefazolin (471 st)	Cefazolin (472 nd)	Cefazolin (473 rd)	Cefazolin (474 th)	Cefazolin (475 th)	Cefazolin (476 th)	Cefazolin (477 th)	Cefazolin (478 th)	Cefazolin (479 th)	Cefazolin (480 th)	Cefazolin (481 st)	Cefazolin (482 nd)	Cefazolin (483 rd)	Cefazolin (484 th)	Cefazolin (485 th)	Cefazolin (486 th)	Cefazolin (487 th)	Cefazolin (488 th)	Cefazolin (489 th)	Cefazolin (490 th)	Cefazolin (491 st)	Cefazolin (492 nd)	Cefazolin (493 rd)	Cefazolin (494 th)	Cefazolin (495 th)	Cefazolin (496 th)	Cefazolin (497 th)	Cefazolin (498 th)	Cefazolin (499 th)	Cefazolin (500 th)	Cefazolin (501 st)	Cefazolin (502 nd)	Cefazolin (503 rd)	Cefazolin (504 th)	Cefazolin (505 th)	Cefazolin (506 th)	Cefazolin (507 th)	Cefazolin (508 th)	Cefazolin (509 th)	Cefazolin (510 th)	Cefazolin (511 st)	Cefazolin (512 nd)	Cefazolin (513 rd)	Cefazolin (514 th)	Cefazolin (515 th)	Cefazolin (516 th)	Cefazolin (517 th)	Cefazolin (518 th)	Cefazolin (519 th)	Cefazolin (520 th)	Cefazolin (521 st)	Cefazolin (522 nd)	Cefazolin (523 rd)	Cefazolin (524 th)	Cefazolin (525 th)	Cefazolin (526 th)	Cefazolin (527 th)	Cefazolin (528 th)	Cefazolin (529 th)	Cefazolin (530 th)	Cefazolin (531 st)	Cefazolin (532 nd)	Cefazolin (533 rd)	Cefazolin (534 th)	Cefazolin (535 th)	Cefazolin (536 th)	Cefazolin (537 th)	Cefazolin (538 th)	Cefazolin (539 th)	Cefazolin (540 th)	Cefazolin (541 st)	Cefazolin (542 nd)	Cefazolin (543 rd)	Cefazolin (544 th)	Cefazolin (545 th)	Cefazolin (546 th)	Cefazolin (547 th)	Cefazolin (548 th)	Cefazolin (549 th)	Cefazolin (550 th)	Cefazolin (551 st)	Cefazolin (552 nd)	Cefazolin (553 rd)	Cefazolin (554 th)	Cefazolin (555 th)	Cefazolin (556 th)	Cefazolin (557 th)	Cefazolin (558 th)	Cefazolin (559 th)	Cefazolin (560 th)	Cefazolin (561 st)	Cefazolin (562 nd)	Cefazolin (563 rd)	Cefazolin (564 th)	Cefazolin (565 th)	Cefazolin (566 th)	Cefazolin (567 th)	Cefazolin (568 th)	Cefazolin (569 th)	Cefazolin (570 th)	Cefazolin (571 st)	Cefazolin (572 nd)	Cefazolin (573 rd)	Cefazolin (574 th)	Cefazolin (575 th)	Cefazolin (576 th)	Cefazolin (577 th)	Cefazolin (578 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th)	Cefazolin (631 st)	Cefazolin (632 nd)	Cefazolin (633 rd)	Cefazolin (634 th)	Cefazolin (635 th)	Cefazolin (636 th)	Cefazolin (637 th)	Cefazolin (638 th)	Cefazolin (639 th)	Cefazolin (640 th)	Cefazolin (641 st)	Cefazolin (642 nd)	Cefazolin (643 rd)	Cefazolin (644 th)	Cefazolin (645 th)	Cefazolin (646 th)	Cefazolin (647 th)	Cefazolin (648 th)	Cefazolin (649 th)	Cefazolin (650 th)	Cefazolin (651 st)	Cefazolin (652 nd)	Cefazolin (653 rd)	Cefazolin (654 th)	Cefazolin (655 th)	Cefazolin (656 th)	Cefazolin (657 th)
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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): 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!

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



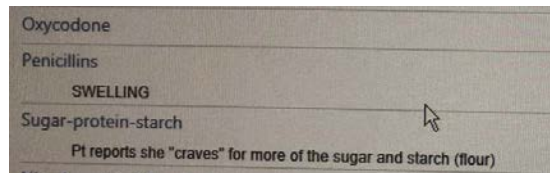
Outline

I. Drug allergies

- Basics
- Beta lactam
- Sulfa
- Fluoroquinolones
- Contrast allergy

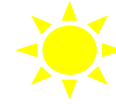
II. Immunodeficiency

III. Anaphylaxis



Sulfonamide Antibiotic Allergy

- Less often IgE mediated reactions, more often mild exanthems
- SULF-FAST criteria less validated than PEN-FAST
- Skin testing is available
- Can consider graded dose oral challenge for non immediate reactions without severe cutaneous symptoms or lab changes.
- NO cross reactivity between TMP-SMX and other non antibiotic sulfonamides including diuretics



Krantz, Matthew S., et al. JACI 2019
Amrol et al. JAMA Netw Open 2019.

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 fluoroquinolones, allergists can often challenge to clarify safety of alternative FQ use
- Skin testing of questionable utility

Fluoroquinolone allergy

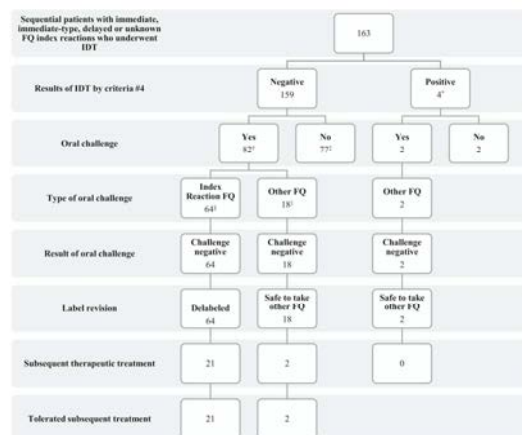


Figure 1

Krantz et al JACIP
2020

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

Outline

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

	Reaction	Severity
Allergies		
Chocolate Flavor	Anaphylaxis	High
Fluticasone	Anaphylaxis	High
Fluticasone Propion-salmeterol	Shortness of Breath, Anaphylaxis, Unknown	High
throat closing		
Orange Juice	Unknown, Photosensitivity, Rash, Anaphylaxis	High
Other	Unknown	High
Quinolones	Unknown, Rash	High
Corn	Unknown	Not Spec
Corticosteroids (Glucocorticoids)	Unknown	Not Spec
Ethinyl Estradiol	Unknown	Not Spec
Lanolin	Unknown	Not Spec
Levofloxacin	Other (See Comments), GI Intolerance	Not Spec
Levonorgestrel	Unknown	Not Spec
Macadamia Nut Oil	Other (See Comments)	Not Spec
Montelukast	Unknown	Not Spec
fatigue		
Naloxone-bupropion	Unknown	Not Spec
Sedation, confusion		
NSAIDs (Non-steroidal Anti-inflammatory Drug)	Other (See Comments)	Not Spec
Sip gastric sleeve, advised minimal use		
Sulfa (Sulfonamide Antibiotics)	Unknown	Not Spec
Adhesive	Rash, Unknown, Swelling	Low
rash from adhesive		
Influenza Virus Vaccine Trivalent 2013-2014 (16 Yr +)	Rash	Low
Influenza Virus Vaccine Trivalent 2013-2014 (16 Yr +)	Rash	Low

10 FOR ADULTS Warning Signs of Primary Immunodeficiency



Primary Immunodeficiency (PI) causes children and adults to have infections that come back frequently or are unusually hard to cure. 1,500 persons are affected by one of the known Primary Immunodeficiencies. If you or someone you know is affected by two or more of the following Warning Signs, speak to a physician about the possible presence of an underlying Primary Immunodeficiency.

- 1 Two or more new ear infections within 1 year.
- 2 Two or more new sinus infections within 1 year, in the absence of allergy.
- 3 One pneumonia per year for more than 1 year.
- 4 Chronic diarrhea with weight loss.
- 5 Recurrent viral infections (colds, herpes, warts, condyloma).
- 6 Recurrent need for intravenous antibiotics to clear infections.
- 7 Recurrent, deep abscesses of the skin or internal organs.
- 8 Persistent thrush or fungal infection on skin or elsewhere.
- 9 Infection with normally harmless tuberculosis-like bacteria.
- 10 A family history of PI.

Presented as a public service by:

Jeffrey Modell Foundation | Caring PI Worldwide | CDC Funding was made possible in part by grant 54T02P220146-05 from the United States Centers for Disease Control and Prevention (CDC)

National Heart, Lung, and Blood Institute (NHLBI) | National Institute of Allergy and Infectious Diseases (NIAID) | National Institute of Child Health and Human Development (NICHD)

Baxter BioScience | CSL Behring | GRIFOLS | octapharma | PPTA | Talecris

These warning signs were developed by the Jeffrey Modell Foundation Medical Advisory Board. Consultation with Primary Immunodeficiency experts is strongly suggested. © 2009 Jeffrey Modell Foundation. For information or referral, contact the Jeffrey Modell Foundation, 800-828-4444, www.jmff.org.

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

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

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

Malignancies

Vaccine responses: pre and post vaccination



Streptococcus pneumoniae Antibodies, IgG (14 serotypes)

PNEUMOCOCCAL SEROTYPE 1, IgG	0.03 ug/mL	0.05 ug/mL
PNEUMOCOCCAL SEROTYPE 3, IgG	0.01 ug/mL	0.11 ug/mL
PNEUMOCOCCAL SEROTYPE 4*, IgG	0.01 ug/mL	0.01 ug/mL
PNEUMOCOCCAL SEROTYPE 5, IgG	0.03 ug/mL	0.03 ug/mL
PNEUMOCOCCAL SEROTYPE 6B*, IgG	0.08 ug/mL	0.05 ug/mL
PNEUMOCOCCAL SEROTYPE 7F, IgG	0.04 ug/mL	0.27 ug/mL
PNEUMOCOCCAL SEROTYPE 8, IgG	0.10 ug/mL	0.06 ug/mL
PNEUMOCOCCAL SEROTYPE 9N, IgG	0.01 ug/mL	0.02 ug/mL
PNEUMOCOCCAL SEROTYPE 9V*, IgG	0.04 ug/mL	0.07 ug/mL
PNEUMOCOCCAL SEROTYPE 12F, IgG	0.03 ug/mL	0.03 ug/mL
PNEUMOCOCCAL SEROTYPE 14*, IgG	0.02 ug/mL	0.04 ug/mL
PNEUMOCOCCAL SEROTYPE 18C*, IgG	0.02 ug/mL	0.02 ug/mL
PNEUMOCOCCAL SEROTYPE 19F*, IgG	0.05 ug/mL	0.04 ug/mL
PNEUMOCOCCAL SEROTYPE 23F*, IgG	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*

My unvaccinated titers: twins in daycare



S. pneumoniae IgG Ab, 23 serotypes, S

Serotype 1 (1)	31.5	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)	27.4	mcg/mL
Serotype 12F (12)	6.9	mcg/mL
Serotype 14 (14)	19.7	mcg/mL
Serotype 17F (17)	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	mcg/mL
Serotype 10A (34)	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)	12.1	mcg/mL

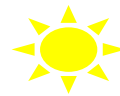
CASE 2: Anaphylaxis



- 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?
- What are the treatment options for food allergies?



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 Up
Follow Up
Follow Up . . .

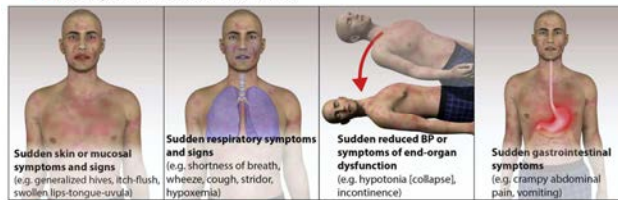
Anaphylaxis

Anaphylaxis is highly likely when any one of the following three criteria is fulfilled

- 1 Sudden onset of an illness (minutes to several hours), with involvement of the skin, mucosal tissue, or both (e.g. generalized hives, itching or flushing, swollen lips-tongue-uvula)



- 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)



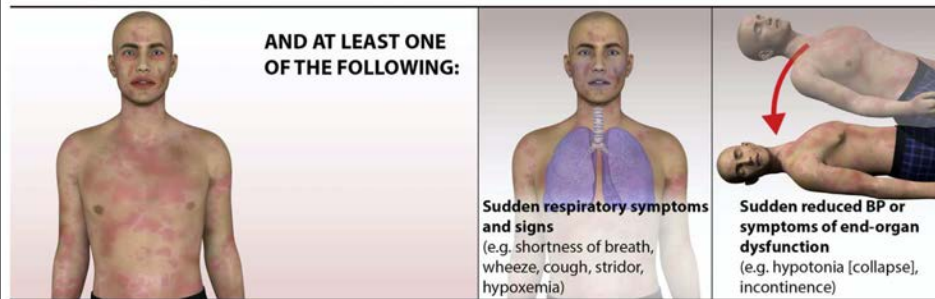
- OR 3 Reduced blood pressure (BP) after exposure to a known allergen** for that patient (minutes to several hours)



Strictest criteria

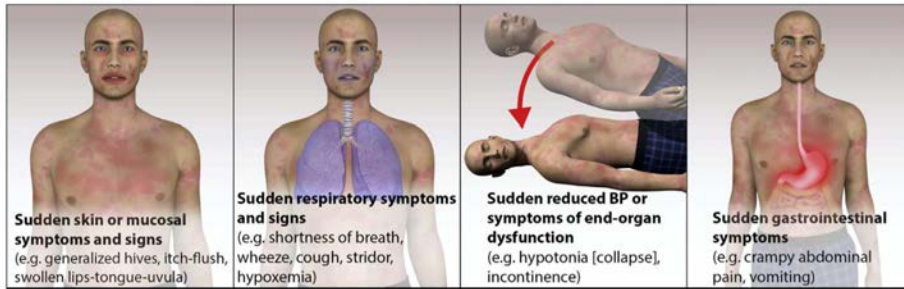
Anaphylaxis is highly likely when any one of the following three criteria is fulfilled

- 1 Sudden onset of an illness (minutes to several hours), with involvement of the skin, mucosal tissue, or both (e.g. generalized hives, itching or flushing, swollen lips-tongue-uvula)





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)



Exposure to patient known allergen

OR 3 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
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Anaphylaxis: Treatment

- 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%



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
- **Stop offending agent** (if its during ingestion, infusion etc)

The epinephrine IM delivery options



Case 2: follow up

- Given Epi IM x1, cetirizine, 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

Food allergies

- Skin and blood testing available for most foods
- For children, oral immunotherapy to certain foods e.g. peanuts and tree nuts is available
- Newer options for adult food allergic patients include FDA approval of omalizumab for accidental exposure
 - Does not eliminate need for food avoidance or carrying epinephrine



Conclusions

- Know what questions to ask to clarify drug allergies
- Understand complexities of penicillin and cephalosporin allergies and the tools to risk stratify patients
- Review sulfa and other antibiotic allergies
- When to call/refer to an allergist
- Anaphylaxis 101
- Spiders can tame lions!

