

Allergy/Immunology: Bootcamp!

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UAB MEDICINE

DEPARTMENT OF PEDIATRICS



Children's
of Alabama

Disclosures

- No commercial financial relationships to disclose
- Operate a 501c3 – Camp WheezeAway

Immunodeficiency

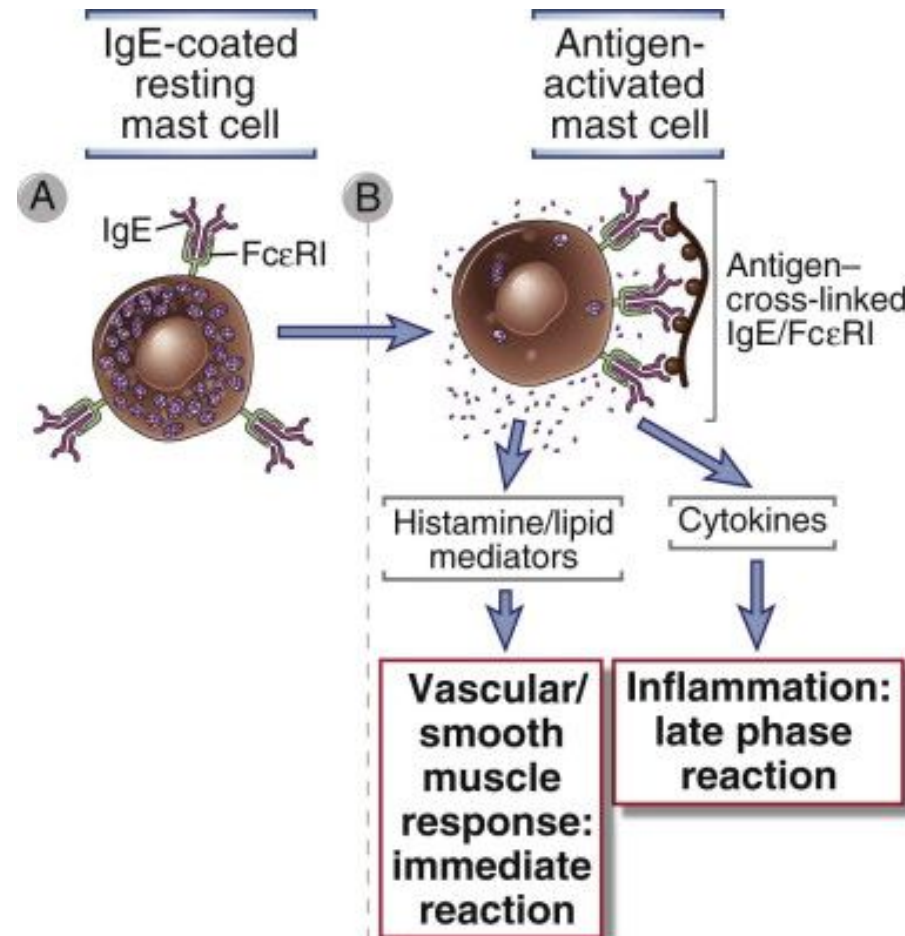
- ★ • Common Variable Immunodeficiency (CVID)
 - 20-40yo with **recurrent sinopulmonary bacterial infections**, 25% with autoimmunity (AIHA, ITP, RA), chronic diarrhea/hx of giardia, hx of IBD
 - Check immunoglobulins and vaccine titers! Low IgG + low IgA and/or IgM
 - Tx: IVIG q3-4 weeks OR SCIG weekly at home
- Selective IgA deficiency
 - @ risk for celiac ~10% of pts, similar presentation to CVID, anaphylactic transfusion reactions
 - Most common immunodeficiency!

Immunodeficiency

- Secondary Hypogammaglobulinemia – medications (rituximab)
- Terminal complement deficiency C5-9 □ recurrent *Neisseria* meningitis
- Chronic granulomatous disease
 - Screening test: neutrophil burst or DHR (dihydrorhodamine)
 - Culprit bugs: nocardia, serratia (catalase + organisms)
 - Invasive abscesses, multifocal osteomyelitis – clues!

Big Picture – The IgE “Allergic” Mechanism

- IgE-mediated
 - Top 8 foods:
 1. Milk – 2.5%
 2. Egg - 2%
 3. Peanut – 1.7%
 4. Tree Nut – 1.7%
 5. Fish
 6. Shellfish
 7. Soy
 8. Wheat
 - Oral Allergy Syndrome
 - Alpha-Gal



You **DO** outgrow...



You **DON'T** outgrow...



Seafood Allergy \neq Contrast Allergy

Badly perpetuated urban myth.























Oral Allergy Syndrome

aka: Pollen-Food Allergy Syndrome

- Pollen-allergic patient eats a food that shares similar epitope with pollen that they are allergic to!
- Sxs: allergic reaction (itching/tingling, swelling) in the mouth/throat)
- Treatment: cook the food, avoidance, allergy shots



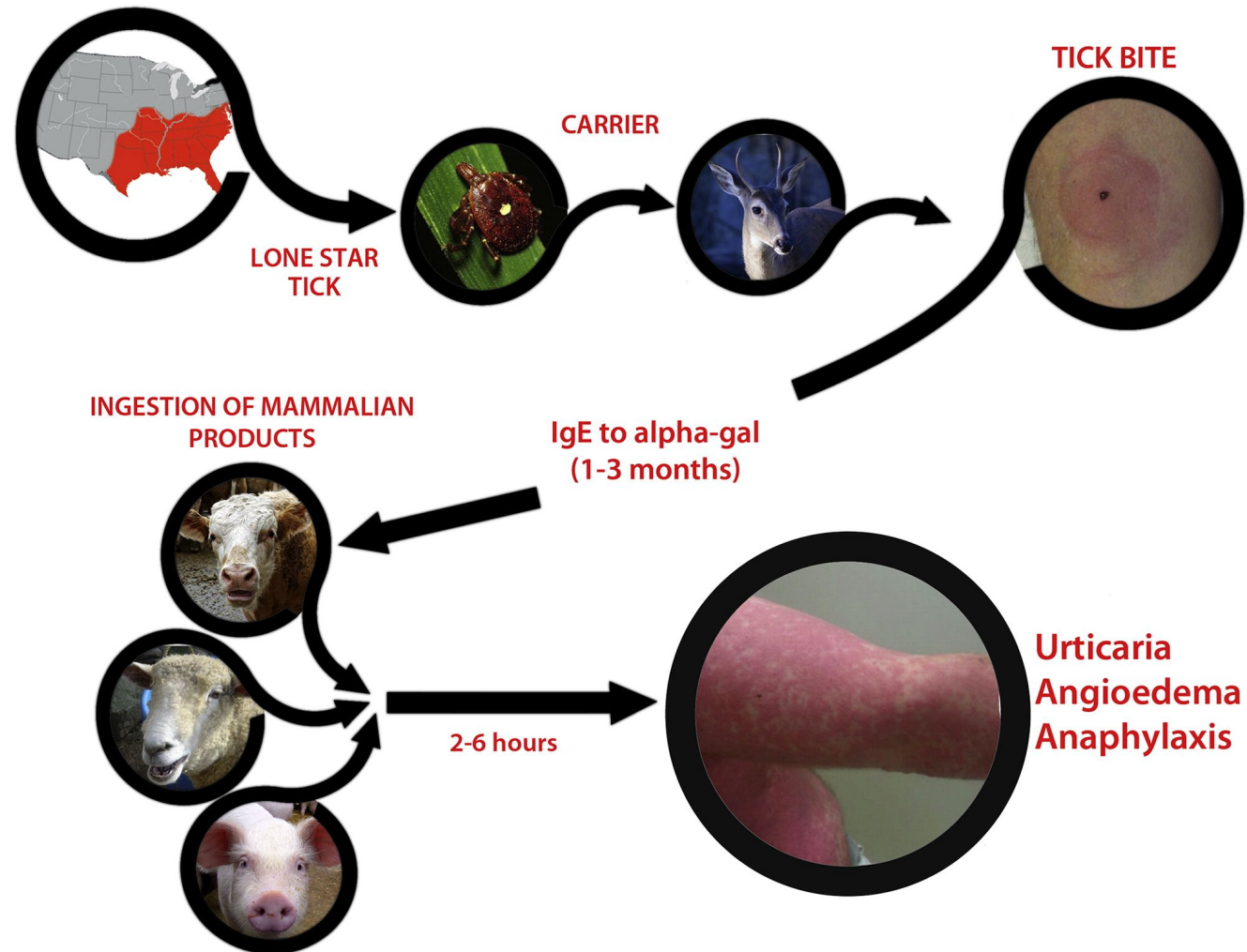
Oral Allergy Syndrome

 Birch	 Rosaceae  Apiaceae	 Fabaceae (old Leguminosae)	 Betulaceae
 Ragweed	 Cucurbitaceae	 Musaceae	
 Mugwort	 Apiaceae  Brassicaceae	 Solanaceae  Liliaceae	 Piperaceae  Rosaceae
 Orchard	 Cucurbitaceae  Fabaceae (old Leguminosae)	 Solanaceae	
 Timothy	 Amaranthaceae  Rutaceae		

CLASSIC:
Apples and
birch pollen...
Ask patient
“Do you eat
apples?”

“Alpha-Gal” Meat Allergy ☐

Delayed Anaphylaxis to Mammalian Meats



IgE “RAST” to
galactose-alpha-1,3-galactose

Venom Hypersensitivity

- BITING insects (Fire ant) vs. FLYING insects (honeybee, yellow jacket..)
- Clinical Symptoms Variable
 - Large local reactions ☐ no VIT; topical/oral steroids, Zyrtec BID
 - Cutaneous systemic (e.g. Generalized hives) ☐ no VIT, Zyrtec BID
 - Systemic ☐ VENOM IMMUNOTHERAPY (VIT) = LIFE SAVING!
- ~10% underlying mastocytosis –
check baseline tryptase



Anaphylaxis Symptoms

- Seconds to minutes after exposure
- The more rapid = the more severe the reaction
- Sometimes prolonged or biphasic
 - Anaphylaxis = cutaneous + 1 other organ system!
 - Cutaneous: pruritus (without a rash), flushing, morbilliform rash, hives, angioedema
 - + CV: hypotension, tachycardia
 - + Respiratory: upper (itchy eyes/nose, rhinorrhea), lower (bronchospasm, wheezing, chest tightness)
 - + GI: N/V, diarrhea

Anaphylaxis Treatment Overview

- Epinephrine

- Epinephrine

- Epinephrine

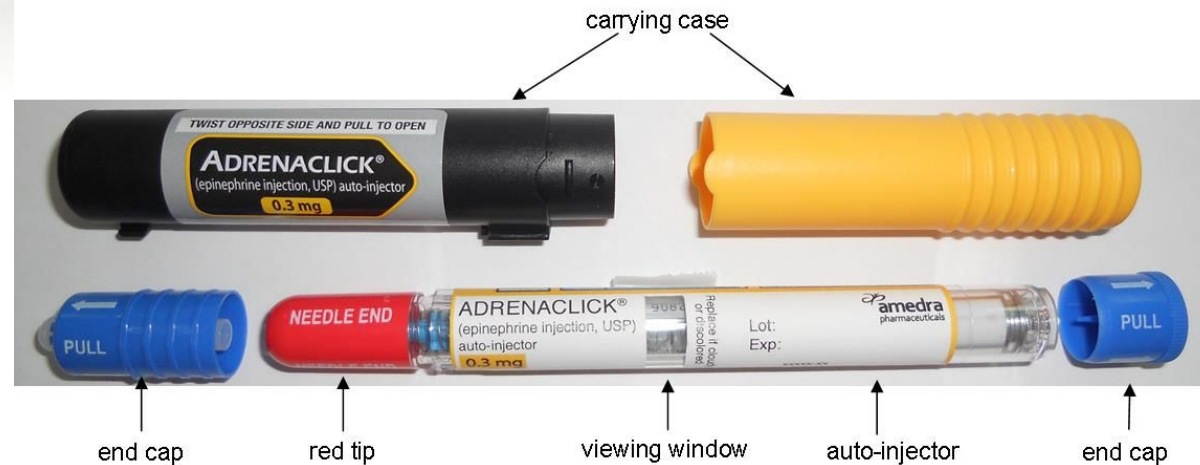
- Epinephrine

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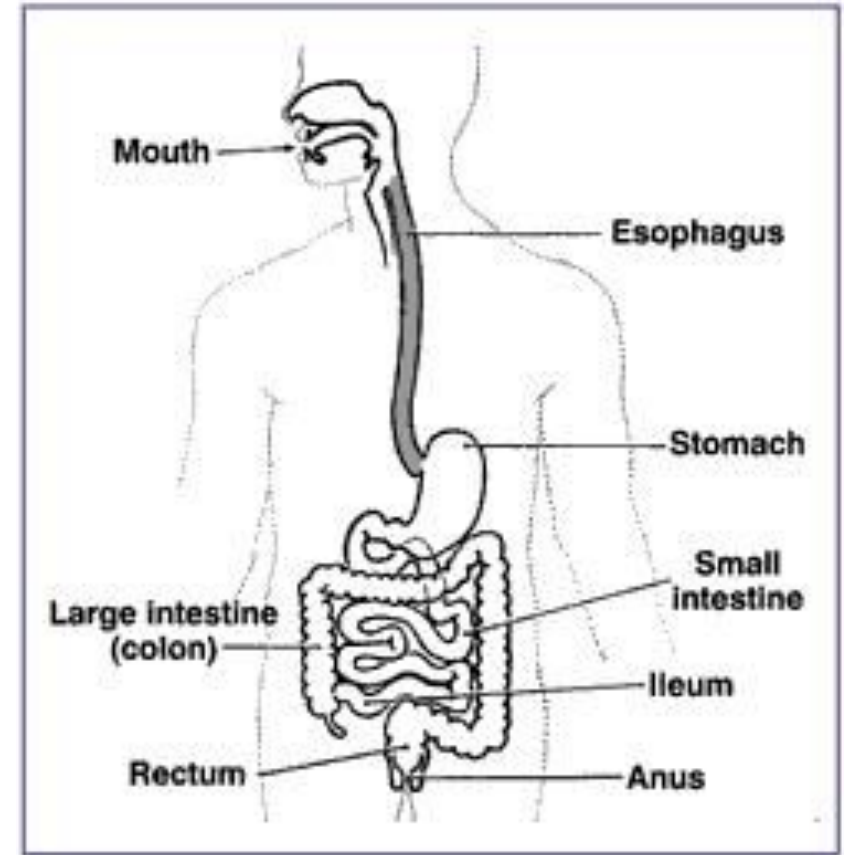
- H1/H2 antihistamines, Steroid, IVF, Albuterol nebs, O₂, Glucagon

Epinephrine Auto-Injectors – 1:1000 IM in the anterolateral thigh



Eosinophilic Esophagitis (EoE)

- Definition: “A chronic, immune/antigen-mediated disease characterized by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation”
- Esophagus is normally devoid of ANY eos – their presence is pathologic!
 - EoE = ≥ 15 eos/hpf
- Mixed IgE and non-IgE mechanisms
- Classic patient: 3:1 male, Caucasian, atopic, family hx of esophageal dilatation



EoE Symptom Review

- Eating or swallowing difficulties
- Chew food carefully
- Last one to leave the table
- Avoidance of confounders – EtOH
- Lots of time spent planning meals
- Cutting foods into small pieces
- Drinking water/adding butter to foods
- Avoidance of bulky foods – meat, bagels

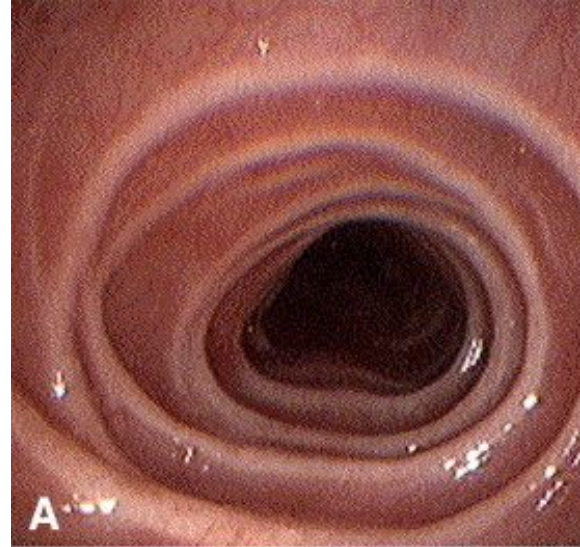
Symptoms:
dysphagia,
food impactions,
chest pain,
hx of esophageal
dilatation,
chronic cough

EGD is a MUST for diagnosis!

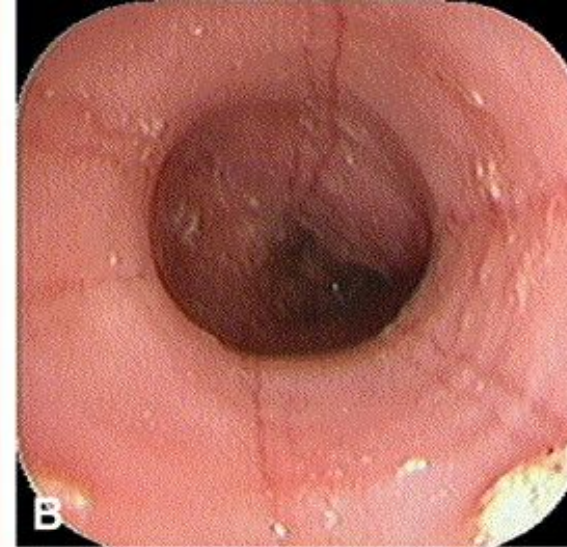
6 total biopsies recommended:
3 prox, 3 distal

**must be off PPI
therapy x4 weeks
before initial EGD!**

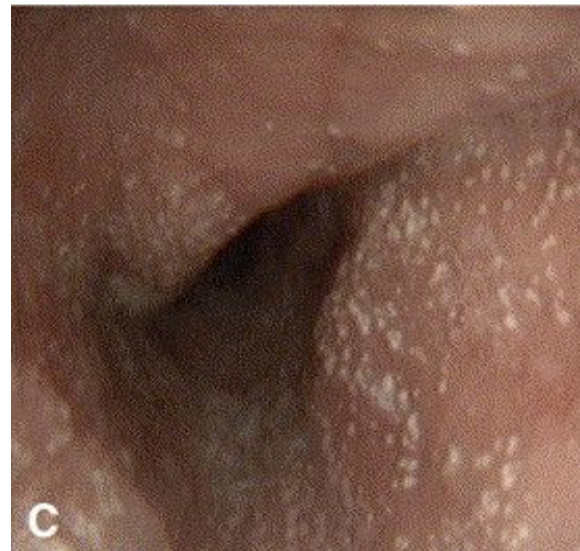
Trachealization



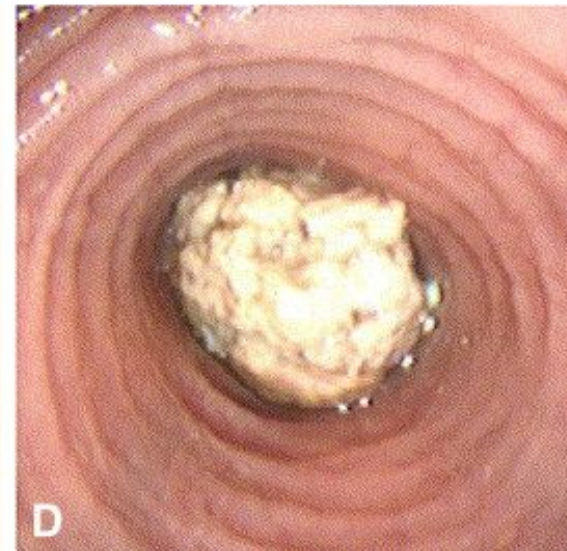
Furrowing



Eosinophilic
Microabscess



Stricture ☐
Food Impaction



Treatment Options

- PPI (1/3 are responders)
- Swallowed steroid – asthma MDI swallowed (ex: flovent) vs. budesonide slurry
- 2 vs 4 vs 6 food elimination diet – all dairy/wheat +/- egg/soy +/- peanut/tree nuts/fish/shellfish
- Dilation of strictures
- Elemental diet
- Biologics (dupilumab > benralizumab, mepolizumab, Xolair) for refractory disease
- As a chronic disease, patient should be educated on need for indefinite therapy!

Asthma

- ~25% of *adult*-onset asthma is occupational related
- Mimics: vocal cord dysfunction!
- **NO ROLE FOR ANTIBIOTICS with exacerbation**
- Pregnancy – rule of 3's! 1/3 get better, 1/3 get worse, 1/3 are stable
 - Avoid excessive SABA use in 1st trimester. **Treat with inhaler>oral steroids if they need it!**
 - **Budesonide** is the only category B med: ICS=Pulmicort flexhaler, ICS/LABA=Symbicort, nasal steroid=rhinocort OTC

Asthma

- 2020 Focused Updates to the Asthma Management Guidelines
 - SMART Therapy (single maintenance and reliever therapy): ICS-Formoterol combination as preventative and rescue inhaler
 - Not to exceed 8 puffs in 4-11yo and 12 puffs in >12yo in a 24 hour period
 - LAMA (long-acting muscarinic antagonist, i.e. tiotropium in all but 1 study) as appropriate add-on therapy to ICS-LABA
- Aspirin-exacerbated respiratory disease (AERD)
 - Samter's triad = nasal polyposis + severe asthma + aspirin allergy
 - Tx: Intranasal steroids - singulair - polypectomy/FESS - aspirin desensitization - dupilumab

Allergic Rhinoconjunctivitis



Denne-Morgan fold
Linear crease or furrows
underneath the lower
eyelids



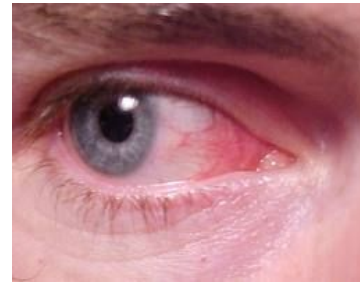
Allergic shiner



Nasal crease



**pale and boggy
inferior turbinate**



conjunctivitis



Cobble stone appearance



Enlarged tonsils and post-nasal drip



**Bulging TM and air-fluid level
due to chronic congestion.
*Eustachian tube dysfunction***

Allergic Rhinoconjunctivitis (ARC)

- Treatment

- Allergen avoidance

- Medications

- ★ • **1st line- nasal steroids**: flunisolide, fluticasone (Flonase), mometasone (Nasonex) , triamcinolone (Nasacort), beclomethasone (Qnasl-powder nasal spray)

- Nasal antihistamine- azelastine, tastes terrible! GREAT for vasomotor rhinitis

- Oral antihistamines-

- loratadine-doesn't work

- Cetirizine (zyrtec), levocetirizine (xyzal) both can make people crazy/sleepy

- Allegra (fexofenadine) works just as well, but won't cause hyperactive behavior, is \$\$\$

- Singulair (Montelukast) – black box warning for mood disturbances

- Anti-histamine/mast cell stabilizing eye drops – avoid Visine!

- Allergen Immunotherapy

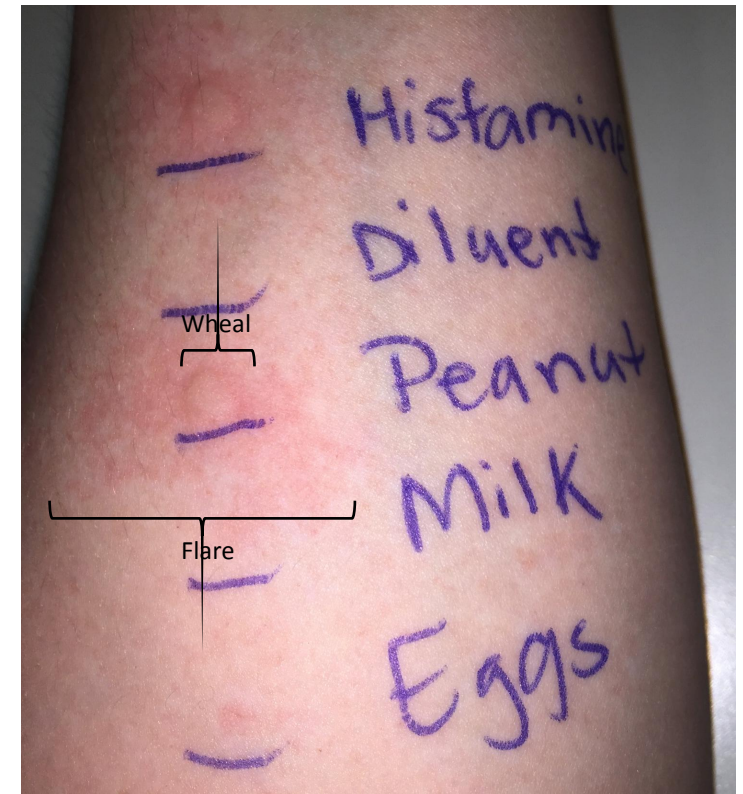
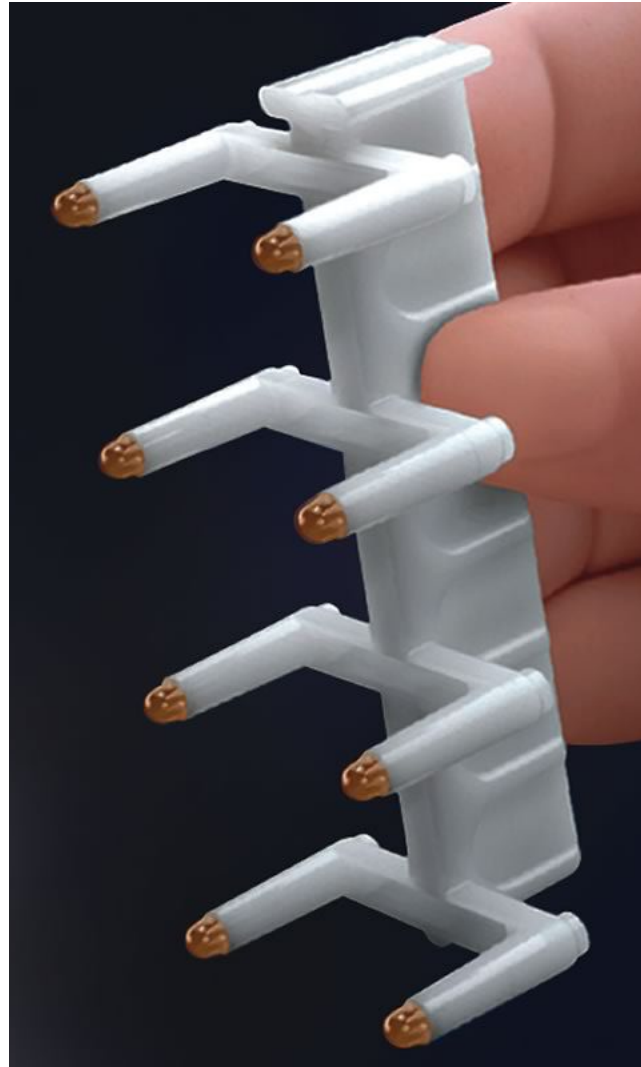
Rhinitis/Sinusitis

- Gustatory rhinitis (induced by eating) – ipratropium nasal spray 30 minutes prior to meals
- Vasomotor rhinitis (non-allergic) – nasal congestion triggered by perfumes/cleaning supplies/smoke
 - Azelastine – anti-histamine nasal spray

Food/Environmental Allergens ☐

Skin Prick Testing

- Histamine: positive control
- Saline: negative control
- **+ result:** wheal $\geq 3\text{mm}$ than negative control
- Can't do if....recent antihistamine use
- 97% NPV, but 50% PPV (foods only)!
- Risk of anaphylaxis if highly-sensitized or uncontrolled asthmatic



Blood Allergy Testing (aka “RAST” or ImmunoCAP)

- Measures specific-IgE levels in the serum
- **Perks:** No anaphylaxis risk, no need to stop antihistamines
- **Downfalls:** two-sided
 - **Positive** serum IgE = sensitization \neq symptomatic food allergy!
 - **Negative** serum IgE \neq no allergy
 - 15-20% false-negative results!

RAST rating	IgE level (KU/L)
0	< 0.35
1	0.35 - 0.69
2	0.70 - 3.49
3	3.50 - 17.49
4	17.50 - 49.99
5	50.0 - 100.00
6	> 100.00

Allergic Contact Dermatitis

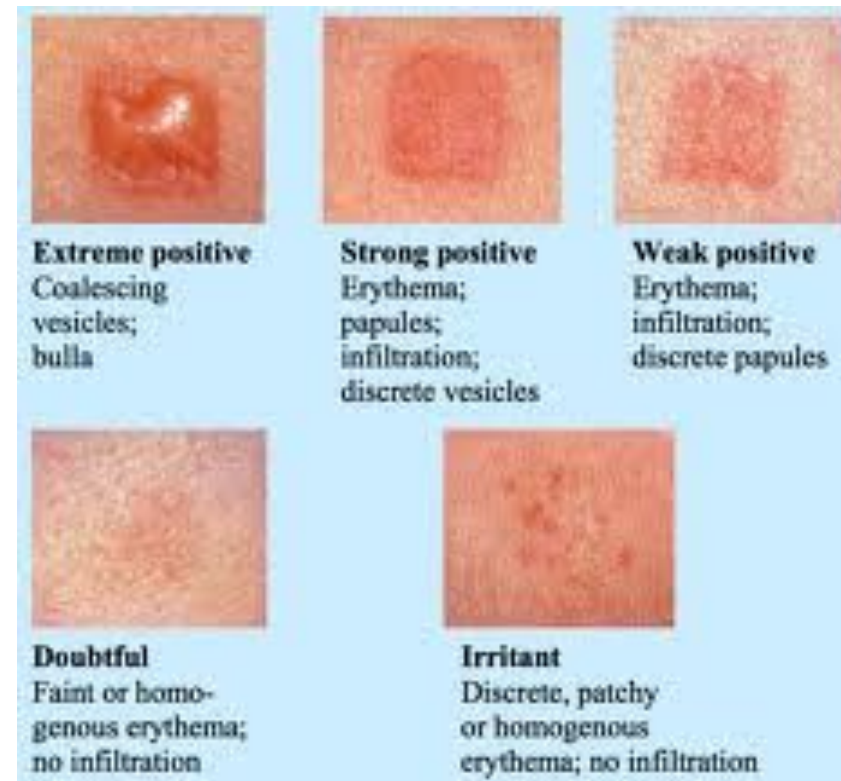


Allergic Contact Dermatitis ☐

Atopy patch testing : APT



- used to diagnose delayed hypersensitivity allergic reaction
 - allergic contact dermatitis
 - Fragrances, hair dye
 - Henna
 - Nickel
 - metal allergy (implants)



Atopic Dermatitis

- DDx: scabies, mycosis fungoides
- Treatment basics
 - Supportive care □ daily bath, MOISTURIZER cream>lotion
 - Control flares □ topical corticosteroids (ointments >>> creams)
 - Do NOT use fluorinated CS on the face, eyelids, groin or skin folds – Only Class VII OK here
 - Wet wraps
 - Dupilumab >6 years of age for resistant cases
- **Do NOT use systemic CS for eczema flares – always the wrong answer; potential for rebound!**



Urticaria/Angioedema

- Angioedema = non-pitting, asymmetric, non-dependent areas
- Urticaria = migratory, transient, v. itchy
- Acute – usually infection-related, <6 wks duration
- Chronic - NO work-up warranted! 85%+ remain idiopathic
- Tx: up to cetirizine 20mg BID; Xolair (omalizumab, anti-IgE biologic) if fail
- Urticarial vasculitis = lesions last >24 hrs, scarring/bruising, burn>itch, poor response to anti-histamines
- Angioedema alone – 11% of cases; ***unusual*** – think drugs (**ACEi, NSAIDs, estrogens**), **SLE or HAE**

Dermatographism

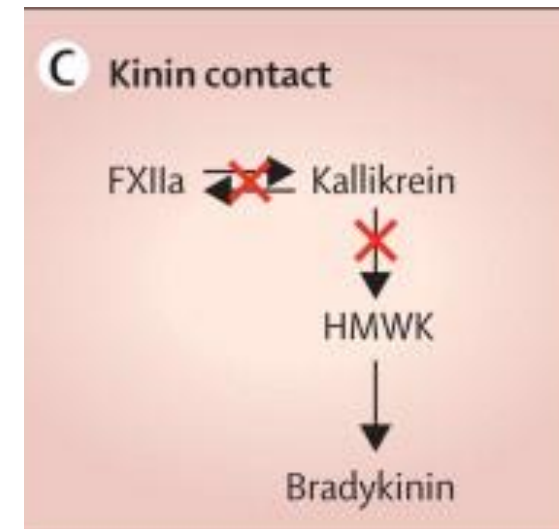




Middletons Fig 37-1

Angioedema Treatment – Acute Attacks

- Bradykinin-mediated swelling (ACEi, hereditary angioedema)
 - C1INH replacement (Berinert) – all ages
 - Ecallantide (Kalbitor) >12yo
 - Icatibant (Firazyr) >18yo
- Histaminergic swelling
 - Steroids
 - Cetirizine 20mg BID >> diphenhydramine
 - (Famotidine 20mg BID)



Drug Allergy – Immune Mediated

- Type I (IgE-mediated)
 - Epinephrine ASAP if acute anaphylaxis!
 - Referral to an allergist for ?skin testing vs. graded-dose challenge/desensitization
 - Skin testing can ONLY be done to IgE-mediated things!
- **NEVER attempt reintroduction/desensitization to Type II-IV...**
 - Type II (Cytotoxic, IgG-med) – HIT, drug-induced neutropenia, hemolysis
 - Type III (Immune Complex) – **serum sickness**, vasculitis, arthrus reaction
 - Type IV (Delayed, T cell-mediated) – SJS/TEN, DRESS

Drug Allergy – Non-Immune Related

- Contrast
- Opiates
- NSAIDs
- Local anesthetics
- Chemotherapeutics (some)
- Monoclonal antibodies
- Vanc – red man syndrome

Drug Allergy – Immune Related

- Allergy Extracts
- Hormones
- Blood Products
- Anesthetic Agents
- ASA/NSAIDS
- Latex
- Chemotherapeutics/Biologics
- Vaccines
- Antimicrobials

COVID Vaccine Allergy

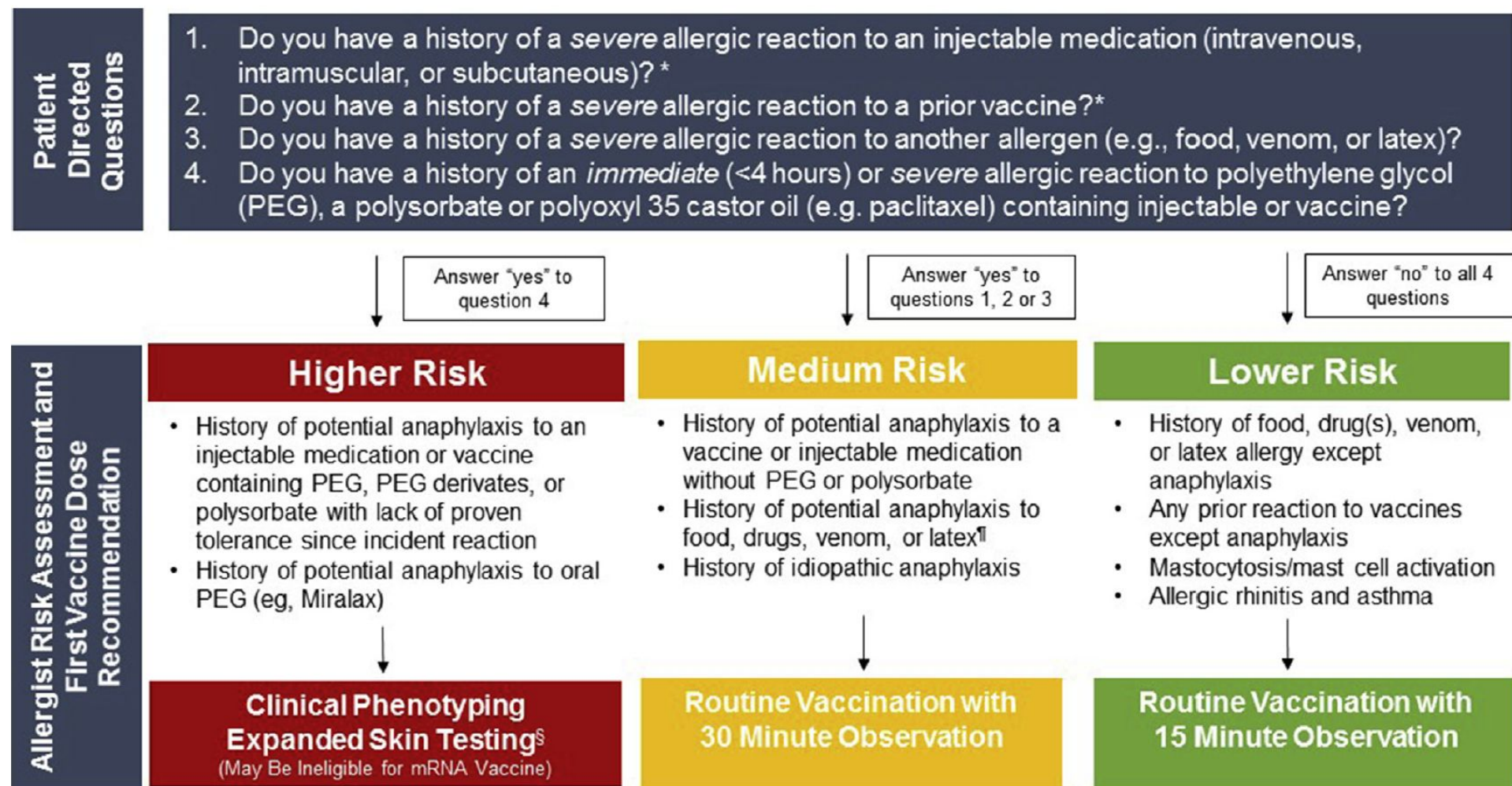
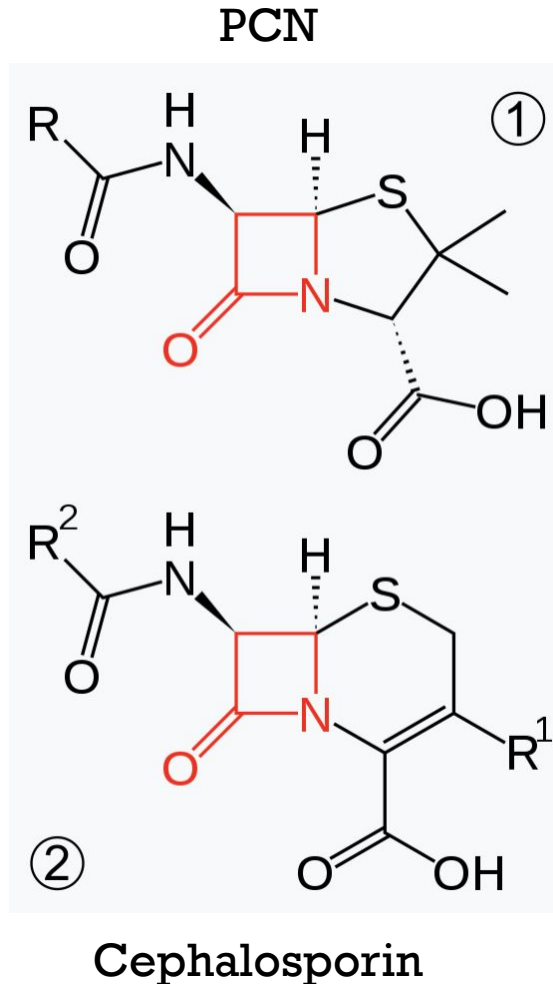


FIGURE 2. Risk stratification pathways with categories based on Mass General Brigham and Vanderbilt allergy expert consensus before initial COVID-19 vaccination. *If “yes” for questions 1 or 2, specific investigation as to the specific injectable products and vaccines should be pursued to determine whether these products could have contained high-molecular-weight PEG, polysorbate, or polyoxyl 35 castor oil (paclitaxel). See [Tables II, III, and IV](#). †Current CDC guidance suggests 30 minutes of observation for patients with any history of anaphylaxis. ‡See [Figures 3 and 4](#) for expanded skin testing procedures and non-irritating skin test concentrations. If skin testing to PEG is positive, as of December 28, 2020, Pfizer-BioNTech and Moderna are the only FDA approved vaccines and under EUA can not be given to an individual with a history of anaphylaxis to a component of the COVID-19 mRNA vaccine. Skin testing to polysorbate 20 and 80 become more important for patients with confirmed severe PEG allergy with regards to the safety of future vaccinations.

Beta-Lactam Allergy



- Cross-reactivity <2%
- Most people outgrow PCN allergy @ rate of 10% per year
- 97-99% of patients found not to be TRULY allergic after testing
- Carrying a “PCN allergy” label on your EHR leads to:
 - ↑ morbidity & mortality
 - ↑ healthcare costs
 - ↑ hospital length of stay
 - ↑ use of broad-spectrum abx (with ↑ \$\$\$)
 - ↑ antimicrobial resistance
 - ↑ rates C.diff, VRE
 - PCN Avoidance □ suboptimal treatment

Allergy is directed at side chains rather than core beta-lactam ring

Table 16. Groups of β -Lactam Antibiotics That Share Identical R₁-Group Side Chains^a

Amoxicillin	Ampicillin	Ceftriaxone	Cefoxitin	Cefamandole	Ceftazidime
Cefadroxil	Cefaclor	Cefotaxime	Cephaloridine	Cefonicid	Aztreonam
Cefprozil	Cephalexin	Cefpodoxime	Cephalothin		
Cefatrizine	Cephradine	Cefditoren			
	Cephaloglycin	Ceftizoxime			
	Loracarbef	Cefmenoxime			

^a Each column represents a group with identical R₁ side chains.

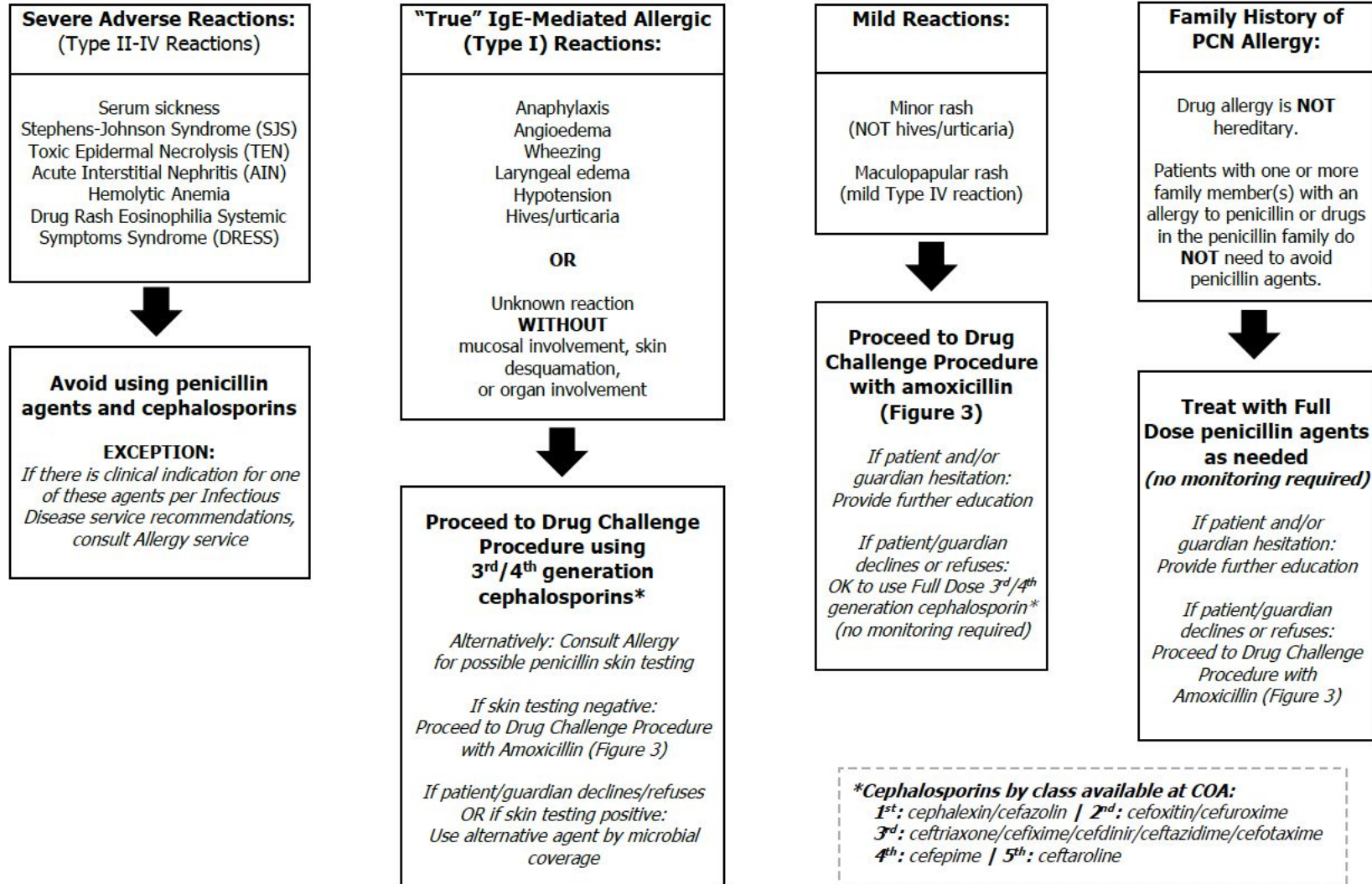
Table 17. Groups of β -Lactam Antibiotics That Share Identical R₂-Group Side Chains^a

Cephalexin	Cefotaxime	Cefuroxime	Cefotetan	Cefaclor	Ceftibuten
Cefadroxil	Cephalothin	Cefoxitin	Cefamandole	Loracarbef	Ceftizoxime
Cephradine	Cephaloglycin		Cefmetazole		
	Cephapirin		Cefpiramide		

^a Each column represents a group with identical R₂ side chains.

UAB Beta-Lactam Allergy Algorithm

Figure 2. COA Penicillin Allergy Algorithm



Thank You! Questions?

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