Learning Objectives

- Epidemiology
- Types of Adverse Drug Reactions
- Types of Hypersensitivity Reactions
  - Diagnosis
  - Management
- Specific Hypersensitivity Reactions

Adverse Drug Events (ADEs)

- Frequency: 4.2/100 admissions
- Cost: $6685 per event
- Serious ADEs \(\rightarrow\) 75,000 – 106,000 deaths per year
- Allergic drug reactions comprise 25% of ADEs
  - Penicillin, amoxicillin, and bactrim most common causes

Drug Allergy

- Most common cause of fatal anaphylaxis in the United States (58%)
- Increasing significantly
  - 0.27 per mill \(\rightarrow\) 0.51 per mill
Terminology is Confusing

Drug Hypersensitivity

Drug Intolerance

IgE mediated reaction

Drug Allergy

Drug Reaction

Adverse Reaction

Sensitivity

Susceptibility

Classification of Adverse Drug Reactions

All unintended pharmacologic effects of a drug
Except: therapeutic failures, intentional overdose, abuse of the drug, or errors in administration

Predictable

Unpredictable

Chemotherapy – Hair Loss

Insulin – Hypoglycemia

Non-IgE Mediated Drug Hypersensitivity Reactions

Penicillin – Anaphylaxis

IgE Mediated (I) Cytotoxic (II) Immune Complex (III) Cell-Mediated (IV) Other Immuneologic

Drug Intolerance

Drug Idiosyncrasy

Pseudoallergic

Other Non-immuneologic

Risk Factors for HSR

- Drug risk factors
  - Chemical properties and molecular weight
  - Dose, route of administration (IV>PO), duration of treatment, repetitive exposure, and concurrent illnesses
    - HIV: allergy to TMP/SMX (bactrim) 9-34%
    - EBV: If patients have EBV and get AMP/AMOX, 30-100% will develop a rash
  - Host risk factors: Age, gender (F>M) and atopy

Classification of Adverse Drug Reactions

Type of reaction

Examples

Predictable

Overdose

Acetaminophen — hepatic necrosis

Side effect

Aspirin — gastric ulcer

Secondary effect

Clindamycin — Clostridium difficile pseudomembranous colitis

Drug-drug interaction

Tobramycin/erythromycin — cardiac arrhythmia

Unpredictable

Insulin

Aspirin — salicylate (oral only)

Idiosyncratic

Diphenylbutylamine in G6PD-deficient patient

Allergic

Penicillin — anaphylaxis

Pseudoallergic

Radiologic contrast media — nephrotoxic reaction

*Abbreviation: G6PD, glucose-6-phosphate dehydrogenase


Adapted from Dr. Aleena Banerji

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Adapted from Dr. Aleena Banerji

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Genetic Risks for Drug Allergy

- HLA-DR3 is associated with increased reactions to insulin, gold, and penicillamine
- HLA-B*5701 is associated with increased reactions to abacavir
- HLA-B*1502 increases risk of Steven Johnson Syndrome/Toxic Epidermal Necrolysis with carbamazepine

Evaluation: Allergy History

- Exact drug, dose and route
- Approximate date of reaction
- Reaction details
  - Doses/days into course
  - Co-administered drugs
  - Coincident infections
  - Symptoms, exam, lab (photos, outside record review)
- Treatment
  - Home, office visit, ED, hospitalization
  - Epinephrine, steroids, antihistamines

Type I, IgE-mediated

- Usually within two hours after drug exposure
- Can recur/worsen with repeat exposure
- Skin testing may be helpful
- If convincing history, or skin test positive, patients may be candidates for desensitization
  - Desensitization induces a state of temporary tolerance through gradual introduction of the drug

Type I, IgE-mediated – Symptoms and Signs

- Cutaneous and mucosal: urticaria, angioedema, pruritus, rhinitis, conjunctivitis
- Gastrointestinal: nausea, throat tightness, difficulty swallowing, vomiting, diarrhea
- Respiratory: cough, dyspnea, wheezing, stridor, hypoxia
- Cardiovascular: hypotension, tachycardia
- Neurologic: confusion, loss of consciousness
Common IgE Exam Findings

- Palmar erythema and pruritus
- Angioedema, often asymmetric
- Urticaria, erythematosus, raised pruritic lesions, with each lesion lasting hours (but <24 hrs)

Evaluation: Skin Testing

- Useful for reactions with possible IgE mechanism
- All patients with an “unknown” reaction may be considered for skin testing to rule out IgE
- No role for skin testing in patients with history of Stevens-Johnson syndrome/toxic epidermal necrolysis, DRESS syndrome, acute interstitial nephritis, exfoliative dermatitis, hemolytic anemia

Evaluation: Skin Testing

- Avoid antihistamines for a minimum of 5 days prior to skin testing
  - Benadryl/diphenhydramine, Allegra/fexofenadine, Claritin/loratadine, etc.
- Hold beta-blockers for 1 day prior to skin testing
  - Blunts response to epinephrine should an anaphylactic reaction occur
- Results are available immediately (15-20 minutes)
Skin Testing – Caveats

- Skin testing for drug allergy is only validated for penicillin allergy where antigenic determinants have been identified.

- All other drug testing can be performed using an established non-irritating concentration with drug challenge being an important part of the evaluation.

Evaluation: Drug Challenges

- Referred to as graded challenge or test dose
- Indicated for low risk patients unlikely to be allergic

- Administration of progressively increasing doses until full dose is reached
  - 1/10th of a dose of IV drug (or 1/4th of a PO drug)
  - followed by 9/10th of a dose of IV drug (or 3/4th of PO)

- Completing a challenge or test dose without an adverse reaction shows there is no immediate (IgE-mediated) drug allergy.

Management: Desensitization

- For reactions that are clinically consistent with IgE mediated hypersensitivity reactions

- Indicated when there is no acceptable treatment alternative
  - must be performed under the supervision of a trained allergist

- Achieved via administering increasing doses of medication in a stepwise manner, such that exposure is continuous

- Induces a state of temporary tolerance though once drug is cleared from system, state of tolerance is lost

Desensitization Protocol Examples

<table>
<thead>
<tr>
<th>Drug Given (mg)</th>
<th>Cumulative Time (min)</th>
<th>Cumulative Drug Dosage (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>5.3</td>
</tr>
<tr>
<td>1</td>
<td>30</td>
<td>1.30</td>
</tr>
<tr>
<td>3</td>
<td>80</td>
<td>4.30</td>
</tr>
<tr>
<td>10</td>
<td>144</td>
<td>14.30</td>
</tr>
<tr>
<td>20</td>
<td>120</td>
<td>34.30</td>
</tr>
<tr>
<td>40</td>
<td>150</td>
<td>74.30</td>
</tr>
<tr>
<td>80</td>
<td>180</td>
<td>152.30</td>
</tr>
<tr>
<td>160</td>
<td>210</td>
<td>317.30</td>
</tr>
<tr>
<td>325</td>
<td>240</td>
<td>642.30</td>
</tr>
</tbody>
</table>

Sample intravenous desensitization (e.g. parenteral antibiotics, chemotherapy)

Sample oral desensitization (to Aspirin 325mg)
Classification of Adverse Drug Reactions

All unintended pharmacologic effects of a drug
Except: therapeutic failures, intentional overdose, abuse of the drug, or errors in administration

* Usually dose-dependent and related to the known pharmacologic actions of the drug

Classification: Hypersensitivity Reactions (HSRs)

Gell & Coombs
- Type I: IgE-mediated (e.g. PCN anaphylaxis)
- Type II: Antibody mediated (e.g. PCN-induced hemolytic anemia)
- Type III: Immune complex (e.g. amoxicillin serum sickness)
- Type IV: Cell mediated (e.g. amoxicillin maculopapular rash)

Non-Immediate Hypersensitivity

- Type II: Hemolytic anemia, neutropenia, thrombocytopenia
- Type III: Serum sickness: fever, rash (MC urticaria), joint pains, high inflammatory markers, low complement

Non-Immediate Hypersensitivity

- Type IV: Morbilliform (maculopapular) rash
  - Onset days into therapy
  - May have peripheral blood eosinophilia
  - Usually benign and self limited
  - Can “treat through” with monitoring
  - May not recur on subsequent exposures
  - Cross reactivity is of less concern
Non-Immediate Hypersensitivity

- Organ specific reactions
  - Immune-mediated nephritis
    - Including acute interstitial nephritis d/t Nafcillin, NSAIDs, ciprofloxacin
  - Immune-mediated hepatitis

- Severe Cutaneous Adverse Reactions (SCARs)
  - Drug Rash Eosinophilia and Systemic Symptoms
  - Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis
  - Erythema Multiforme

Severe Cutaneous Adverse Reactions (SCARs)

- Drug Rash Eosinophilia and Systemic Symptoms
  - High mortality (5-40%)
  - Clinical criteria, AEC > 1500/mL, rash, and systemic involvement (fever, LAD, hepatitis, nephritis)
  - Anticonvulsants, antimicrobials, sulfasalazine, NSAIDs, ACE inhibitors, Beta blockers, dapsone, allopurinol, azathioprine, diltiazem, methimazole, dobutamine
  - Stevens-Johnson syndrome/toxic epidermal necrolysis
    - Mucous membrane involvement
    - Mortality 5-40%
    - Causative agents: allopurinol, antiepileptics, NSAIDs, sulfa-containing antibiotics, and nevirapine

Specific Drug Reactions

- Beta-lactam antibiotics
- Sulfonamide antibiotics
- Radio contrast media
- Aspirin/NSAIDs
- ACE inhibitors

Antibiotics

- Beta-lactam antibiotics
- Sulfonamide antibiotics
- Radio contrast media
- Aspirin/NSAIDs
- ACE inhibitors
Antibiotics are widely used in United States

- 4.2-5.7% of outpatient population between 1999 to 2012
- 50% of inpatients
- penicillins and cephalosporins = top 2 sold in the United States
- 60% of all the antibacterial drug market

Kantor JAMA 2015
Magill JAMA 2014

Inaccurate PCN allergy label → Adverse Outcomes
10-15% report PCN allergy

Inpatients with reported PCN allergy
- Longer Stays
  - 10% more days in the hospital
- 20-30% more drug-resistant infections
  - 23% more C diff, 14% more MRSA, 30% more VRE
- > 90% are not PCN-allergic

PCN allergy can be addressed easily using validated diagnostic tests

Penicillin Allergy & Use of Broad-Spectrum Antibiotics

Antibiotic Costs in “Penicillin Allergic” Patients

<table>
<thead>
<tr>
<th>Study</th>
<th>Cost – Penicillin Allergic Patients</th>
<th>Cost – No Penicillin Allergic</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kraemer MJ (1997)</td>
<td>$4.6</td>
<td>$1.75</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MacLaughlin EJ (2000)</td>
<td>$28.6</td>
<td>$16.3</td>
<td>0.004</td>
</tr>
<tr>
<td>Sade K (2003)</td>
<td>$81.7</td>
<td>$52.5</td>
<td>0.015</td>
</tr>
<tr>
<td>Sade K (2003)</td>
<td>$43.0</td>
<td>$31.0</td>
<td>&lt;0.0005</td>
</tr>
</tbody>
</table>

1. Average antibiotic costs per patient during 24 month period
2. Average antibiotic costs per patient (one course)
3. Average antibiotic costs per day during hospitalization
4. Average antibiotic costs per day – post-hospitalization treatment
The Cost Problem of Penicillin Allergy

- Total cost of antibiotics prescribed for patients with penicillin allergy was 1.82-2.58-fold higher than for first-line antibiotics.
- During in-hospital treatment, the mean antibiotic cost for penicillin-allergic patients was 63% higher.
- Cases with penicillin "allergy" averaged 0.59 (CI, 0.47-0.71) more total hospital days during 20 months of follow-up.

PCN Allergy Evaluation

- Graded challenge (test dose) with penicillin antibiotic (amoxicillin) is gold standard.
- Skin testing:
  - reduces number of positive test doses.
  - Serum-specific IgE not accurate.

PCN Skin Testing has a NPV > 95%

PCN Skin Testing Performed with PCN & PCN G

PRO (use minor determinants)
- Only 1 more positive oral challenge per 3375 individuals.
- Positive oral amoxicillin challenges of equal or less severity than food and aspirin challenges.

CON (minor determinants not needed)

Aminopenicillins: Unique R-group Side Chains

- Amoxicillin oral challenge identifies patients sensitized only to minor determinants or R group side chain

Penicillin Allergy Referrals

- Any patient with penicillin allergy can benefit
- Patients who specifically benefit include patients with:
  - Recurrent infections/hospitalization
  - Current or past infection where best therapy includes a beta-lactam
  - Planned surgical procedure where a beta-lactam antibiotic is the drug of choice
  - Upcoming chemotherapy or transplantation

Penicillin Skin Testing: Effect on Antibiotic Use

<table>
<thead>
<tr>
<th>Study</th>
<th>% Pen ST Negative</th>
<th>Effect on Broad Spectrum Antibiotic Use (% of Patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harris AD (1999)</td>
<td>86%</td>
<td>Vancocin 20% - 0% Quinolones 27% - 14%</td>
</tr>
<tr>
<td>Arroliga ME (2003)</td>
<td>89%</td>
<td>Vanco/Quinolones 100% - 68%</td>
</tr>
<tr>
<td>Nadarajah K (2005)</td>
<td>92%</td>
<td>Vancomycin 77% - 8% Quinolones 28% - 3%</td>
</tr>
<tr>
<td>Park M (2006)</td>
<td>96%</td>
<td>Vancomycin 39% - 19%</td>
</tr>
<tr>
<td>del Real GA (2007)</td>
<td>88%</td>
<td>Vancomycin 37% - 18% Quinolones 36% - 13%</td>
</tr>
<tr>
<td>Frigas E (2008)</td>
<td>?</td>
<td>Vancomycin 28% - 10%</td>
</tr>
</tbody>
</table>

PCN Skin Testing is Cost-effective

- Annual salary of RN who can perform 8 PCN allergy tests per 8-hour shift: $118,000
- Dose of penicilloyl-polylysine (Pre-Pen): $69.00
- Amoxicillin 250 mg tablet: $0.12
- All other necessary supplies: $3.25
- Total per patient: $131.37

PCN allergy testing of 146 inpatients

- Acute antibiotic costs:
  - $32,811 ($225/patient) reduction over 5 months
- $82,000 annual estimated difference
PCN Skin Testing is Cost-effective

- Total cost of antibiotics prescribed for patients with penicillin allergy 1.82-2.58-fold higher than for first-line antibiotics
- Inpatient: mean antibiotic cost for penicillin-allergic patients was 63% higher
- Cases with penicillin “allergy” averaged 0.59 (CI, 0.47-0.71) more total hospital days during 20 months of follow up

Estimated cost of PCN skin testing 51,582 patients with PCN “allergy”

\[ \text{Estimated cost} = \text{Estimated savings} \]

\[ \frac{\$6.8 \text{ million}}{0.59 \text{ days per patient}} = \$64.6 \text{ million} \]

Need for Improved EHR Allergy Documentation

36% (20/55) patients had PCN allergy re-documented

- Age, long-term care facility, altered mental status, dementia

Guideline Based Evaluation of PCN Allergy

- Guideline to assist providers with assessing allergy history and prescribing antibiotics for patients with reported penicillin or cephalosporin allergy
- Used a standard 2-step graded challenge or test dose
- Compared treatment 21 months before guideline implementation with 12 months after guideline implementation

Guideline Based Evaluation of PCN Allergy: Outcomes

- Almost 7-fold increase in the number of test doses to β-lactams

Significantly decreased treatment with alternative antibiotics

- Vancomycin 68 \( \rightarrow \) 37%
- Aztreonam 12 \( \rightarrow \) 5%
- Aminoglycosides 6 \( \rightarrow \) 1%
- Fluoroquinolones 15 \( \rightarrow \) 3%
- No difference in adverse drug reactions
Cephalosporin Allergy

- Hypersensitivity occurs in 0.0001-3% of administrations
- R group side chain is major factor for cross-reactivity between PCN and cephalosporins

Cephalosporin: Cross-reactivity with PCN

- ~2% cross reactivity between PCN and 1st generation oral cephalosporins
- <1% for PCN and 2nd/3rd/4th generation cephalosporins

Patient selectively allergic to aminopenicillins should avoid cephalosporins with common R group side chain

Cross-reactivity between cephalosporins Based on Side Chain Similarity

PCN Cross-reactivity with Carbapenems and Aztreonam

- <1% of PCN-allergic patients react to carbapenem
- PCN-allergic patients tolerate aztreonam
- Ceftazidime cross-reacts with aztreonam
Sulfonamide Antibiotics

- Reported in 1.5–3% of patients
  - Often cause minor Type IV reactions
  - Most common cause of Steven Johnson Syndrome/Toxic Epidermal Necrolysis

- Patients with a sulfonamide antibiotic allergy may be safely prescribed other medications from the non-antibiotic sulfonamide class of drug

- No validated skin testing available

Radiocontrast Media (RCM)

Risk Factors for Contrast Reactions

- **Risk Factor**
  - Age: 20–50 years old
  - History of prior reaction
  - Comorbidities
    - Cardiovascular disease
    - Asthma
    - Atopy
  - β-blocker use

- **What is affected?**
  - Any reaction
  - Life-threatening reaction
  - Any reaction
  - Reaction with bronchospasm
  - Any reaction
  - Any reaction
  - Any reaction
  - Any reaction
  - Reaction with bronchospasm
  - Any reaction

- **Numbers**
  - 15.18% reaction rate
  - OR 7.71; 95% CI 1.04–57.23
  - OR 8.74; 95% CI 2.36–32.35
  - OR 16.39; 95% CI 4.30–62.46
  - 2 times more likely
  - 4 times more likely
  - 3.73; 95% CI 1.18–11.75
  - OR 15.75; p=0.023
  - Hypotension
  - Hazard of overall reaction

Iodinated Contrast Media Widely Used

- Millions of studies / year
- Reaction rate: 13% → 3-5% with low-osmolar contrast

- Risk factors
  - 20 – 50 years of age
  - History of prior reactions
  - Comorbidities
    - Cardiovascular disease
    - Asthma
    - Atopy
  - β-blocker use
The ‘iodine/seafood allergy’ Myth

Osborne treats syphilis with iodine-containing compounds \rightarrow notices urine is radio-opaque

1922: First pyelogram performed at Mayo Clinic

Dolan JAMA 1940: 2 deaths following the intravenous use of diodrast

2015: 86% physicians at academic medical centers incorrectly think iodine and seafood sensitize patients to contrast

Studies establish that ‘iodine allergy’ does not sensitize patients to contrast

1983: Girard & Gamba: iodine and seafood sensitize patients to contrast

1980: Kaufman EJIM: ‘iodine allergy’ does not sensitize patients to RCM

1990: Stukus AAAI: ‘iodine allergy’ does not sensitize patients to RCM

1940: Studies establish that ‘iodine allergy’ does not sensitize patients to RCM

1920-1940: First pyelogram performed at Mayo Clinic

1940: Goldburgh JAMA: 2 deaths following the intravenous use of diodrast

1983: Girard & Gamba: iodine and seafood sensitize patients to contrast

1990: Stukus AAAI: ‘iodine allergy’ does not sensitize patients to RCM

1940: Studies establish that ‘iodine allergy’ does not sensitize patients to RCM

Low-osmolar Non-ionic Has Lower Reaction Rates Compared To High-osmolar Ionic Contrast

**TABLE 3: Multicenter Surveillance Studies: Reactions to Contrast Media**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Conventional Media</th>
<th>Nonionic Media</th>
<th>Relative Risk Conventional/Nonionic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall prevalence of reactions</td>
<td>12.7</td>
<td>3.1</td>
<td>4.1</td>
</tr>
<tr>
<td>Katayama et al. [8]</td>
<td>3.8</td>
<td>1.2</td>
<td>3.0</td>
</tr>
<tr>
<td>Low risk</td>
<td>10.3</td>
<td>1.3</td>
<td>7.5</td>
</tr>
<tr>
<td>High risk</td>
<td>4.1</td>
<td>0.7</td>
<td>5.9</td>
</tr>
<tr>
<td>Prevalence of severe reactions</td>
<td>0.22</td>
<td>0.04</td>
<td>5.5</td>
</tr>
</tbody>
</table>

RADIOCONTRAST MEDIA

Premedication Prevents Recurrent Reactions

- Use Visipaque dye (nonionic, iso-osmotic)
- Prednisone 50mg every 6 hours for 3 doses (13 hours, 7 hours, and 1 hour before RCM)
- Benadryl 50mg 1 hour before RCM
Risk Factors for Breakthrough Reactions (BTR)

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Breakthrough Group</th>
<th>Control Group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergic Rhinitis</td>
<td>21</td>
<td>8</td>
<td>.04</td>
</tr>
<tr>
<td>Food Allergy</td>
<td>29</td>
<td>8</td>
<td>.007</td>
</tr>
<tr>
<td>Hay fever</td>
<td>3</td>
<td>4</td>
<td>.003</td>
</tr>
<tr>
<td>Oral allergy, 4+ allergens</td>
<td>3</td>
<td>4</td>
<td>.003</td>
</tr>
</tbody>
</table>

Majority of BTRs Same / Milder Severity Compared to Initial Reaction

<table>
<thead>
<tr>
<th>Reference</th>
<th>Pretreatment Regimen</th>
<th>% of BTR more severe than initial reaction (severe reactions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freed 2001</td>
<td>Prednisone 20mg p.o. every 6 hours for 5 doses before RCM</td>
<td>11% (0 severe)</td>
</tr>
<tr>
<td>Davenport 2009</td>
<td>Prednisone 50mg p.o. every 6 hours for 3 doses before RCM</td>
<td>8% (1 severe)</td>
</tr>
<tr>
<td>Bae 2013</td>
<td>Prednisone 200mg i.v. 1 hour before RCM</td>
<td>5% (1 severe)</td>
</tr>
</tbody>
</table>

< 1 % patients have severe BTR

Contrast Reactions: Take-home Points

- Initial reaction rate 3-5% with low-osmolar contrast
- Risk factors:
  - Prior reactions, heart disease, asthma, atopy, β-blocker use
- Premedication:
  - Use Visipaque dye (nonionic, iso-osmotic)
  - Prednisone 50mg every 6 hours for 3 doses (13 hours, 7 hours, and 1 hour before RCM)
  - Benadryl 50mg 1 hour before RCM

Specific Drug Hypersensitivities

- NSAIDs
- ACE inhibitors
- Penicillin
- Neomycin
- Diabetic
- Lactose
- Respiratory
NSAID Reactions

- 25-30% of patients taking NSAIDs
- 0.5% to 5.7% in the general population
- Allergic Reactions
- Pseudo-allergic Reactions

Allergic NSAID Reactions
- Mechanism: IgE-mediated
- Induced by a single NSAID

Pseudo-allergic Reactions
- Type 1 – asthma and rhinosinusitis
- Type 2 – urticaria/angioedema in patients with chronic urticaria
- Type 3 – urticaria/angioedema in otherwise asymptomatic individuals

ACE Inhibitor Reactions

- Angioedema occurs in 0.1% to 0.7% of patients treated with ACE inhibitors
- 4 to 5-fold higher risk in African Americans, females, and older age
- Most common cause of angioedema seen in the hospital and emergency room

- Usually presents as angioedema of the face and neck (throat, tongue, lips, eyes)
- Bradykinin-mediated → therapies targeting bradykinin pathway (like Firazyr) are useful

ACE Inhibitor Angioedema

- Mechanism: COX enzyme inhibition
- Induced by class of NSAIDs
- Most patients tolerate acetaminophen and selective COX-2 inhibitors (e.g. celecoxib)
### Drug Allergy Special Testing Clinic

- 5-HT3 Receptor Antagonists
- Anesthetic
- General & Local
- Antibiotics
  - Aminoglycosides
  - Beta-Lactams
  - Cephalosporins
  - Clindamycin
  - Macrolides
  - Quinolones
  - Vancomycin
- Benzyl Alcohol
- Chemotherapy
- Disinfectant/Antimicrobial
- Diuretics
- Immunomodulators
- Glatiramer Acetate
- H2 Blockers
- Heparins
- Insulin
- IV Contrast Agents
- Monoclonal Antibodies
- Ophthalmic Agents
- Polyethylene glycol
- Progesterone
- Proton Pump Inhibitors
- Steroids
- Vitamin B12
- Vaccines
- Xolair

### Key Take-Home Points

- Hypersensitivity reactions are a small subset of adverse drug reactions
- If allergy is suspected, a careful drug allergy history and physical exam is the best next step and can usually help to distinguish between HSRs that are common or severe
- Skin testing, challenges/test doses, and desensitization can be performed by allergists to help in the diagnosis and treatment