Drug Allery: Evaluation and Management with Updated Guidelines

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Disclosures

- Presenter has no relevant or material financial interest in any of the medications or organizations mentioned in the presentation.

- Baylor University has not evaluated the information contained in this presentation.

Drug Allergies (and other HSRs)

- Classified based on
  - Chronology—Timeline of Events
  - Mechanism—What process is occurring
  - Clinical Presentation—What symptoms are occurring
- All reactions often lumped into allergy

Drug Allergies and HSRs

- IgE mediated reactions
  - Quick onset
  - Urticaria, Angioedema, Bronchospam, Anaphylaxis

Hypersensitivity Reactions

- Often Delayed—Days to Weeks
  - Morbilliform Drug Eruption
  - Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)
  - Acute Generalized Exanthematous Pustulosis (AGEP)
  - Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis (SJS/TENS)
  - Serum Sickness-Like Reaction (SSLR)

Antibiotic Allergies

- Pennicillin
  - Rare (10% of US claims allergy, less than 1% have it)
  - PCN allergy label is common and not benign
    - Leads to Increase in cost and drug toxicity
    - Can lead to less effective treatment
  - Testing vs Challenge

Antibiotic Allergy

- PCN Allergy Recommendations
  - Proactive de-labeling of PCN allergy
  - No testing for low-likelihood allergy or long-ago reaction—Challenge
  - Reserve skin testing for likely or severe reactions
  - Discourage multi-day challenges
  - No testing before failed challenge in pediatrics presenting with urticaria

Antibiotic Allergy

- Cephalosporins
  - Reactivity largely related to R1 chains
- Symptoms present with reaction determines how to proceed.

Antibiotic Allergy

- Cephalosporin Allergy Recommendations
  - For low risk reactions to PCN or cephalosporins, may use dissimilar R1 chains or challenge if patient prefers and is not emergent
  - For hx of anaphylaxis or for similar R1 chain, test patients prior to challenge

Antibiotic Allergy

Beta-Lactam Cross-Reactivity

-Classify Anaphylactic vs Not and Verified vs Not

Reaction	**OK to Use**
PCN-Urticaria	Cephalosporins
PCN-Anaphylaxis	Non-Cross Reactive Cephalosporins
Cephalosporins-Urticaria	PCN
Cephalosporins-Anaphylaxis	Test/Challenge PCN before use

Antibiotic Allergy

- Beta-Lactam Allergy Recommendations
  - Patients with anaphylaxis to PCN may have dissimilar cephalosporins without testing or challenge
  - No additional testing or challenge necessary for patients with reaction to PCN or cephalosporins for Carbapenem use
  - Specialists recommended to work with healtcare systems to increase pathways to utilize beta-lactams.

Antibiotic Allergy

- Sulfonamides
  - Delabeling is helpful for immunocompromised patients
  - For low risk or distant reactions, proceed straight to challenge with TMP-SMX
    - Greater than 5 years previous—1-step challenge
    - More recent that 5 years—2-step challenge

Antibiotic Allergy

- Fluoroquinolones
  - For distant or low risk reaction proceed to 1-step challenge
  - For severe or recent reaction proceed to 2-step challenge with different fluoroquinolone.

Antibiotic Allergy

- Macrolides
  - Low likelihood of allergy
  - Direct challenge okay in most patients
  - No contraindication for PCN/Cephalosporin allergy unless has had reaction to Aztreonam.

NSAID Hypersensitivity

- 4 Categories based on history, underlying disease, anaphylaxis, and/or other organ system involvement
  - Aspirin Exacerbated Respiratory Disease (AERD)
  - NSAID Induced Urticaria/Angioedema
  - NSAID Exacerbated Cutaneous Disease
  - Single NSAID Induced Reaction

NSAID Hypersensitivity

- AERD
  - Clinical history sufficient for diagnosis
  - Challenge okay in cases of uncertainty
  - Desensitize ASA when needed for cardiovascular protection

NSAID Hypersensitivity

- NSAID Induced Urticaria/Angioedema
  - No underlying disease to exacerbate
  - May react to all COX-1 inhibitors
  - Use selective COX-2 inhibitors as alternative if needed

Khan, et al; Kowalski, et al

NSAID Hypersensitivity

- NSAID Exacerbated Cutaneous Disease
  - History of urticarial disease
  - Can typically be treated with H1 antihistamines or omalizumab
  - 2-step challenge ASA for non-AERD

Khan, et al; Kowalski, et al

NSAID Hypersensitivity

- Single NSAID Induced Reaction
  - IgE mediated immediate vs delayed
  - Typically not related to COX-1 inhibition
    - May use other NSAIDs

Khan, et al; Kowalski, et al

Chemotherapy Reactions

- Managing Chemotherapy HSR
  - Desensitization if drug is preferred vs alternative medication
  - Risk stratification based on reaction and drug necessity
  - Skin testing to assist risk stratification
  - Avoidance and use of alternative drug if appropriate

Chemotherapy Reactions

- Patinum-based agents
  - Severity of reaction can help risk determination
  - Skin testing to assist in risk stratification
- Taxanes
  - Reaction usually from excipient
- Tyrosine Kinase Inhibitors (TKIs)
  - Rare Allergy
  - Manage symptomatically

Khan, et al

Reaction to Biologics

- Agents created from living cells, tissues, or other organisms
- Reactions include IgE-mediated, mast cell activation, SSLR
- Testing rarely indicated
  - For patients with immediate reaction or anaphylaxis, may desensitize if drug is preferred.
  - Fore mild reactions, slow infusion or graduated dosing. Khan, et al

Reaction to Biologics

- Rituximab
  - Highest risk of reaction to initial dose
  - Greater than 77% of patients with B-cell lymphoma will have reaction
  - Managed with slowing infusion or desensitization
  - Risk of reaction decreases with subsequent doses

Reactions to Biologics

- Cetuximab
  - Reactions primarily associated with alpha-gal sensitivities
- Infliximab
  - Risk highest on initial exposures
  - Also may be related to alpha-gal

Reaction to Biologics

- Omalizumab
  - Relatively low risk of reaction
  - Reactions most likely on 1st or 2nd exposure
  - May cause delayed reaction
    - 36% of reactions over 1 hour after administration
    - 7% of reactions over 12 hours after administration

Excipients

- Inactive substances alongside active ingredients in medications
  - More likely sensitivity than allergy
  - Although a rare cause of allergy, may be considered source in cases of multiple unrelated drug allergies with the same excipient

Drug Challenges

- First recommendation when likelihood of allergy is low or mild reaction
  - Consider when reaction was, what symptoms, what drug, number of listed allergies for the patient
  - For more likely reactions, but unclear, still may challenge if benefit of drug outweighs risk
  - Contraindicated in severe reactions

Drug Challenges

- Recommendations
  - In cases with low clinical probability of reaction, proceed directly to challenge
  - In cases with inconsistent symptoms or multiple listed allergies, can consider placebo challenge

Testing for Delayed Reactions

- Little evidence present for any available methods
- Can consider IDT or patch testing as adjunct testing in decision making on a case-by-case basis

Takeaways

- Aggressive delabeling of PCN allergy
- Communicate delabeling of PCN allergy to patients entire health team to avoid reacquisition of label
- Majority of cases are appropriate for challenge as first step
- Reserve drug allergy testing for severe allergy and high-likelihood cases

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