APPROACH TO COMMON DRUG ALLERGIES

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Any noxious, unintended and undesired effect of a drug that occurs at doses used in humans for diagnosis, prevention, or treatment.
EPIDEMIOLOGY

• ADRs account for 3%-6% of all hospital admissions and occur in 10%-20% of hospitalized patients.
• Drug allergy accounts for up to 20% ADRs.
• Drug allergy, occurs in 1%-2% of all admissions and 3%-5% of hospitalized patients, respectively.

EPIDEMIOLOGY

• The true incidence of drug allergy in the community is unknown; it’s been reported in 8% of population
• Many patients are misdiagnosed as being “allergic” to various medications, particularly antibiotics, and end up carrying this label
• These patients are frequently treated with alternate medications that may be more toxic, less effective and more expensive

# Types of Hypersensitivity Reactions

<table>
<thead>
<tr>
<th>Type</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>IgE-mediated</td>
<td>Antibody-mediated</td>
<td>Immune complex-mediated</td>
<td>T-lymphocyte-mediated</td>
</tr>
<tr>
<td>Onset</td>
<td>Immediate (minutes – hours)</td>
<td>Delayed (days to weeks)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reaction examples</td>
<td>Anaphylaxis  <strong>Urticaria (hives)</strong>  Angioedema  Wheezing  Shortness of breath  Syncope  Cardiac arrest</td>
<td>Hemolytic anemia  Thrombocytopenia  Neutropenia</td>
<td>Serum sickness  Vasculitis</td>
<td>Maculopapular rash  Fixed drug eruption  Contact dermatitis  <strong>SCAR</strong>  - DRESS  - SJS  - TEN  - AGEP  Acute interstitial nephritis  Drug-induced liver injury</td>
</tr>
</tbody>
</table>

SCAR: Severe cutaneous adverse reactions  
AGEP: Acute generalized exanthematous pustulosis  
DRESS: Drug rash with eosinophilia and systemic symptoms  
SJS: Stevens—Johnson syndrome  
TEN: Toxic epidermal necrolysis
Mast cell activation

Fluoroquinolone urticaria

Penicillin angioedema
ASPIRIN ALLERGY
## TABLE I. Classification of NSAID-induced hypersensitivity reactions

<table>
<thead>
<tr>
<th>Timing of reaction</th>
<th>Clinical symptoms</th>
<th>Cross-reactivity within NSAID class</th>
<th>Presence of underlying disease</th>
<th>Putative mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>AERD</td>
<td>Acute Rhinitis, nasal congestion, bronchoconstriction, asthma exacerbation</td>
<td>Cross-reactive</td>
<td>Asthma/rhininosinusitis/nasal polyps</td>
<td>COX-1 inhibition</td>
</tr>
<tr>
<td></td>
<td>Multiple NSAID-exacerbated urticaria/angioedema in patients with underlying cutaneous disease</td>
<td>Cross-reactive</td>
<td>Chronic urticaria</td>
<td>COX-1 inhibition</td>
</tr>
<tr>
<td>Multiple NSAID-induced urticaria/angioedema in otherwise asymptomatic patients</td>
<td>Acute Urticaria/angioedema</td>
<td>Cross-reactive</td>
<td>None</td>
<td>Likely COX-1 inhibition</td>
</tr>
<tr>
<td>Acute</td>
<td>Urticaria/angioedema</td>
<td>Cross-reactive</td>
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<td></td>
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<tr>
<td>Single NSAID-induced anaphylactic reactions</td>
<td>Anaphylaxis, urticaria/angioedema</td>
<td>Single drug-induced</td>
<td>Atopy is common</td>
<td>IgE-mediated</td>
</tr>
<tr>
<td>Acute</td>
<td>Urticaria/angioedema</td>
<td>Cross-reactive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delayed reactions to NSAIDs</td>
<td>Varied: Fixed drug eruptions, severe bullous skin reactions, maculopapular drug eruptions</td>
<td>Can be single drug-induced or cross-reactive</td>
<td>None</td>
<td>Varied: T-cell—mediated, cytotoxic T cells, natural killer cells, other</td>
</tr>
</tbody>
</table>
ACE-induced angioedema
**Tongue angioedema**

<table>
<thead>
<tr>
<th>Lips borders clearly visible</th>
<th>Palate and uvula partially not visible</th>
<th>Small space between lips and tongue</th>
<th>Tongue completely fills mouth office</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>Grade II</td>
<td>Grade III</td>
<td>Grade IV</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>Hospitalization</td>
<td>Hospitalization</td>
<td>Hospitalization</td>
</tr>
<tr>
<td>Intensive care</td>
<td>Intensive care</td>
<td>Intensive care</td>
<td>Intensive care</td>
</tr>
</tbody>
</table>
Laryngeal angioedema

- 25% obstruction of supralarynx: Grade LOC I
- 50% obstruction of supralarynx: Grade LOC II
- 75% obstruction of supralarynx: Grade LOC III
- 90% obstruction of supralarynx: Grade LOC IV
LYMPHOCYTE ACTIVATION

Clinical Phenotype

- **DRESS, 2-to-8-week delay:**
  Epidermal edema, fever, lymphadenopathy, eosinophilia, atypical lymphocytosis, and infiltration of skin and internal organs

- **SJS–TEN, 4-to-28-day delay:**
  Epidermal necrosis, subepidermal bullae, and involvement of multiple mucous membranes

- **AGEP, 24-to-48-hour delay:**
  Fever, neutrophilic leukocytosis, sterile pustules in stratum corneum and epidermis, dermal edema, and infiltration of neutrophils, CD4+ T cells, CD8+ T cells, and some eosinophils
VIRAL VS. DRUG RASH

Diagnosis

- Measles (rubeola)

- Rubella

- Roseola infantum (exantheme subitum)

- Erythema infectiousum (fifth disease)

- Infectious mononucleosis

- Acute graft-versus-host disease

- Acute human immunodeficiency virus seroconversion

- Other viral exanthems
Acute Contact Dermatitis and Photoallergic Dermatitis
Fixed Drug Eruption

Fixed drug eruption (a) Extensive disease showing pigmented macules, some with blistering (b) bullous variant resembling SJS and (c) acute fixed drug eruption showing indurated oedematous plaques.
Acute Generalized Exanthematous Pustulosis

Acute generalized exanthematous pustulosis (AGEP) (a) classic flexural pustules (b) small pustules on a background of indurated erythema.

Drug-Induced Vasculitis

Vasculitis showing (a) palpable purpura on the lower legs and (b) a more severe variant showing blisters and ulceration.

Lichenoid drug reaction (LDR) showing (a) pigmented macules (b) violaceous erythema of the lips and (c) recurrence on re-exposure to the same drug. The depigmented area represents original sequelae of LDR and the violaceous areas developed on re-exposure to the drug.
Symmetrical drug-related intertriginous and flexural exanthem

- Within the first 2 days of exposure
- Symmetrical erythematous lesions involving the flexural intertriginous and gluteal areas

https://doi.org/10.1016/j.clindermatol.2020.06.013
Drug Reaction, Eosinophilia, and Systemic Syndrome (DRESS)

Japanese Consensus Group

1) Maculopapular eruption developing >3 weeks after starting a limited number of drugs
2) Prolonged clinical symptoms 2 weeks after discontinuation of the causative drug
3) Fever (>38°C)
4) Liver abnormalities (alanine aminotransferase [ALT] >100 U/L)*
5) Leucocyte abnormalities (at least one present)
   - Leukocytosis (>11 x 10^9/L),
   - Atypical lymphocytosis (>5%)
   - Eosinophilia (>1.5 x 10^9/L)
6) Lymphadenopathy
7) HHV-6 reactivation
Polymorphous maculopapular eruption (85%) and facial edema (76%); pustules, purpura, infiltrated plaques, blisters, target-like lesions, urticarial lesions, an exfoliative dermatitis, eczema-like lesions, and lichenoid lesions
• Symptoms may worsen after the drug therapy is discontinued and may persist for weeks or even months
• Reported DRESS syndrome mortality rates worldwide are approximately 10%
• Some patients develop late-onset sequelae such as myocarditis or autoimmune conditions even years after the initial cutaneous eruption

A.R. Cardones MD, Drug reaction, eosinophilia, and systemic symptoms (DRESS) syndrome, Clinics in Dermatology (2020)
### Table 2. Short and long-term sequelae of DRESS/DIHS

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthritis</td>
</tr>
<tr>
<td>Arthralgia, reactive arthritis, rheumatoid arthritis</td>
</tr>
<tr>
<td>Autoimmune thyroiditis</td>
</tr>
<tr>
<td>Colitis / enteropathy</td>
</tr>
<tr>
<td>Cutaneous autoimmune disease</td>
</tr>
<tr>
<td>Vitiligo, alopecia areata</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Encephalitis</td>
</tr>
<tr>
<td>Fulminant hepatic failure</td>
</tr>
<tr>
<td>Hemolytic anemia</td>
</tr>
<tr>
<td>Myocarditis</td>
</tr>
<tr>
<td>Pneumonitis</td>
</tr>
<tr>
<td>Renal failure</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
</tr>
<tr>
<td>Venous thrombosis</td>
</tr>
</tbody>
</table>

### Table 3. Common causes of DRESS/DIHS

<table>
<thead>
<tr>
<th>Category</th>
<th>Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-gout medications</td>
<td>Allopurinol</td>
</tr>
<tr>
<td>Anti-microbials</td>
<td>Abacavir, Dapsone, Minocycline, Nevirapine, Trimethoprim-sulfamethoxazole, Vancomycin</td>
</tr>
<tr>
<td>Anti-epileptics</td>
<td>Carbamazepine, Lamotrigine, Phenytoin, Phenobarbital</td>
</tr>
<tr>
<td>Anti-inflammatory medications</td>
<td>Sulfasalazine</td>
</tr>
</tbody>
</table>

A.R. Cardones MD, Drug reaction, eosinophilia, and systemic symptoms (DRESS) syndrome, Clinics in Dermatology (2020)
SERUM SICKNESS & SERUM SICKNESS-LIKE REACTION

- Urticaria, polycyclic plaques, or a morbilliform exanthem.
- Skin eruptions (90%), arthritis (52%), fever (41%), arthralgia (38%), abdominal pain (21%), and lymphadenopathy (10%).
- Low complement levels in true serum sickness

Drug Reactions with Bullae

- Fixed drug eruption
- Bullous pemphigoid
- Pemphigus vulgaris
- Linear IgA bullous dermatosis
- SJS/TEN

SJS & TEN

- Onset 4 to 21 days after first dose of drug
- Mucous membranes nearly always involved with blisters and erosions
- Temperature >38.5°C, systemic signs initially
- Severe, acute blistering; initially, rash may be macular erythema or exanthem on the trunk
- Extent of epidermal necrosis according to body-surface area:
  - 10 -30% in SJS–TEN overlap
  - < 10% in SJS
  - >30% in TEN

Pediatrics Vol. 146, Issue 31 Sep 2020
ERYTHEMA MULTIFORME

https://www.nidirect.gov.uk/conditions/erythema-multiforme
EM & SJS

Multiforme E. Journal Of Advances In Allergy & Immunologic Diseases, Volume 1, Issue 1, 2015
BETA-LACTAM ALLERGY
URTICARIA VS. MACULOPAPULAR RASH

A

B

C

D

A penicillin-allergy label is usually acquired in childhood.

Up to 20% of the population engaged in medical care is labeled as penicillin-allergic.

**Personal Health Implications**
- Fewer efficacious antibiotic choices
- More toxic effects associated with alternative antibiotics
- Use of broad-spectrum antibiotics
- More postoperative surgical-site infections

**Public Health Implications**
- Antibiotic resistance
- Higher rates of *C. difficile* infection
- Use of more costly antibiotics
- Increased length of hospital stays

**Formal Allergy Assessment**
<5% Labeled as allergic to penicillin are truly allergic.
Harms associated with use of non-β-lactam antibiotics

Increased use of 2nd-line antibiotics
- Vancomycin
- Aztreonam
- Fluoroquinolones
- Clindamycin

Increased use of unnecessarily broad-spectrum antibiotics
- Meropenem

- ↑ mortality
- ↑ treatment failures
- ↑ adverse effects (e.g. nephrotoxicity, QTc prolongation)
- ↑ colonization and/or infection with resistant pathogens
  - Methicillin-resistant Staphylococcus aureus (MRSA)
  - Vancomycin-resistant enterococci (VRE)
  - Clostridium difficile
- ↑ surgical site infections

**Diagnosis**

**A. Epicutaneous**
- Histamine
- Saline
- 15 min

**B. Intradermal**
- Histamine
- Saline
- PPL
- 15 min

**C. Patch**
- In place for 48 h
- Negative
- Positive
  - Amoxicillin 10%
  - Petrolatum control
  - Ampicillin 10%
  - Cephalaxin 10%

**D. Intradermal**
- Ampicillin 25 mg/mL
- 24 h

**Research for Limited Use**
- Basophil activation testing
- Serum-specific IgE

**Drug challenge** (positive skin test excluded)
- Single or full dose
- Graded

**Drug challenge** (severe rash and single organ disease excluded)
- Single or full dose
- Multiple day

**Lymphocyte transformation testing**
- ELISPOT assay for drug-specific T cells
- HLA typing or other pharmacogenetic risk allele testing
PENICILLIN TESTING-YES

- Skin testing evaluates only for IgE-mediated reactions
- IgE-mediated reactions wane over time: 80% no longer allergic after 10+ years
- Low cross-reactivity with cephalosporins (2%)
PENICILLIN TESTING - NO
Don’t overuse non-beta-lactam antibiotics in patients with a history of penicillin allergy, without an appropriate evaluation.
β-lactam Cross Reactivity

Heatmap of similarities between R1 side chains.

<table>
<thead>
<tr>
<th>Cephalosporins</th>
<th>Penicillin G</th>
<th>Penicillin V</th>
<th>Ampicillin</th>
<th>Amoxicillin</th>
<th>Cloxacillin</th>
<th>Piperacillin</th>
<th>Ticarcillin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefadroxil</td>
<td>0.371</td>
<td>0.220</td>
<td>0.018</td>
<td>1.000</td>
<td>0.179</td>
<td>0.060</td>
<td>0.333</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>0.592</td>
<td>0.333</td>
<td>1.000</td>
<td>0.618</td>
<td>0.208</td>
<td>0.043</td>
<td>0.371</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>0.176</td>
<td>0.110</td>
<td>0.099</td>
<td>0.088</td>
<td>0.078</td>
<td>0.032</td>
<td>0.088</td>
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<tr>
<td>Cefradine</td>
<td>0.344</td>
<td>0.200</td>
<td>0.517</td>
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<td>0.155</td>
<td>0.082</td>
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<tr>
<td>Cephalothin</td>
<td>0.563</td>
<td>0.321</td>
<td>0.337</td>
<td>0.295</td>
<td>0.154</td>
<td>0.035</td>
<td>0.268</td>
</tr>
<tr>
<td>Ceftrazime</td>
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<td>0.220</td>
<td>0.618</td>
<td>1.000</td>
<td>0.179</td>
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<td>0.035</td>
<td>0.268</td>
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<thead>
<tr>
<th>Cephalosporins</th>
<th>Penicillin G</th>
<th>Penicillin V</th>
<th>Ampicillin</th>
<th>Amoxicillin</th>
<th>Cloxacillin</th>
<th>Piperacillin</th>
<th>Ticarcillin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefaclor</td>
<td>0.592</td>
<td>0.333</td>
<td>1.000</td>
<td>0.618</td>
<td>0.208</td>
<td>0.043</td>
<td>0.371</td>
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<tr>
<td>Cefotaxin</td>
<td>0.330</td>
<td>0.245</td>
<td>0.211</td>
<td>0.180</td>
<td>0.148</td>
<td>0.043</td>
<td>0.180</td>
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<tr>
<td>Cefprozil</td>
<td>0.371</td>
<td>0.220</td>
<td>0.618</td>
<td>1.000</td>
<td>0.179</td>
<td>0.060</td>
<td>0.333</td>
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<tr>
<td>Cefuroxime</td>
<td>0.304</td>
<td>0.220</td>
<td>0.274</td>
<td>0.248</td>
<td>0.320</td>
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<td>Cefamandole</td>
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<td>0.333</td>
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<td>Cefixime</td>
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<td>0.110</td>
<td>0.098</td>
<td>0.157</td>
<td>0.219</td>
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<td>0.138</td>
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<td>0.182</td>
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<tr>
<td>Ceftazidime</td>
<td>0.092</td>
<td>0.097</td>
<td>0.099</td>
<td>0.142</td>
<td>0.198</td>
<td>0.064</td>
<td>0.127</td>
</tr>
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<td>Ceftriaxone</td>
<td>0.141</td>
<td>0.090</td>
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<td>0.249</td>
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<tr>
<td>Cefdinir</td>
<td>0.147</td>
<td>0.083</td>
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<td>0.156</td>
<td>0.207</td>
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<td>0.238</td>
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<tr>
<td>Ceftibuten</td>
<td>0.167</td>
<td>0.127</td>
<td>0.148</td>
<td>0.165</td>
<td>0.237</td>
<td>0.079</td>
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<td>0.090</td>
<td>0.138</td>
<td>0.142</td>
<td>0.249</td>
<td>0.049</td>
<td>0.182</td>
</tr>
</tbody>
</table>
**APPENDIX B3. Table of β-Lactam Cross-Reactivity**

β-lactam cross-reactivity is primarily thought to be predicted based on shared R1 and R2 side chains between antibiotics.

Patient can exhibit hypersensitivity reactions to non-cross reacting antibiotics based on other mechanisms.

<table>
<thead>
<tr>
<th>Penicillins</th>
<th>Penicillin</th>
<th>Amoxicillin</th>
<th>Ampicillin</th>
<th>Nafcillin</th>
<th>Oxacillin</th>
<th>Ticloxacin</th>
<th>Piperacillin/tazobactam</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st Generation Cephalosporin</td>
<td>Cefadroxil</td>
<td>Cephalexin</td>
<td>Cefaclor</td>
<td>Cefprozil</td>
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<td>Cefdinir</td>
<td>Cefixime</td>
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<td>3rd Generation Cephalosporin</td>
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<td>Aztreonam</td>
<td>Aztreonam</td>
<td>Aztreonam</td>
<td></td>
</tr>
</tbody>
</table>

* Increased potential for cross-reactivity
STRATIFY RISK

High
- Mucosal involvement (e.g., SJS) or profound skin desquamation
- Organ (e.g., kidney) involvement or vital sign change
- Emergency visit or hospital admission
- Epinephrine use
- Rash with high or protracted fever
- Parenteral steroid use
- Skin biopsy performed
- Oral steroid use
- Cutaneous symptoms only
- Antihistamines used
- Remote reactions (>10 years ago)
- No therapy was needed
- Itching only
- Tested positive without exposure
- Non-allergic symptoms (e.g., headache)
- Family history only

Low
Conduct **THOROUGH History / Patient Interview**

**Interview patient**

- ✓ Medication – name of medication
- ✓ Age – how old when reaction occurred
- ✓ **REACTION** – describe reaction
  - ▪ If hives, prompt itchy, raised welts/wheels
- ✓ **ONSET** – how many days into therapy did reaction occur
- ✓ **TREATMENT** – drug discontinuation, antihistamine, ED visit, hospitalization
- ✓ **DURATION** – how long reaction lasted
- ✓ Other medications tolerated
  - ▪ Prompt “Augmentin, Keflex, Omnicef, ceftriaxone (Rocephin), cefepime (Maxipime) and/or specific β-lactams identified upon chart review
Differentiating Cutaneous Drug Reactions

**Urticaria (hives)**
- Fast onset (minutes to hours)
- Raised off skin
- Pruritic
- Duration < 24 hours
- No scarring

**Benign rash**
- Delayed onset (days)
- Less pruritic than urticaria
- Duration >24 hours
- Fine desquamation with resolution over days to weeks

**SCAR**
- Delayed onset (days to weeks)
- Blistering / desquamation
- Mucosal and/or organ involvement
- Hospitalization

Update the Electronic Health Record

Type: Allergy

*Substance
amoxicillin

Reaction(s):
(tolerated cefazolin)

*hives

*Severity
<not entered>

At: <not entered>

Onset: Year
2004

Info source:
Patient

Comments:
9/10/2019 8:52 PM - Reaction: hives, itchy, lots of diarrhea
Onset: 1st day
Treatment: drug discontinuation
Duration: < 24 hours
Desensitization versus Graded Challenge

**Desensitization**
- Administering the offending agent at a concentration and rate that will cause drug-specific IgE-armed mast cells to degranulate at low rates without causing an allergic reaction, and ultimately allow for the drug to be administered at a full therapeutic dose
  - “Temporary drug tolerance”

**Graded Challenge**
- Administering 1-2 TEST doses to rule-out the presence of IgE-mediated reaction
  - “Test dose procedure: 10%, wait 1 hour, then administer 100%”
## Desensitization versus Graded Challenge

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Desensitization</th>
<th>Graded Challenge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Description</td>
<td>Temporary drug tolerance</td>
<td>TEST dose procedure</td>
</tr>
<tr>
<td>Risk of IgE-mediated hypersensitivity reaction (i.e. anaphylaxis)</td>
<td>High (e.g. history of anaphylaxis)</td>
<td>Low-Moderate</td>
</tr>
<tr>
<td>Location</td>
<td>ICU</td>
<td>Any unit</td>
</tr>
<tr>
<td>Ordered by</td>
<td>Allergy/ID</td>
<td>Any prescriber</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Allergy/ID consult recommended)</td>
</tr>
<tr>
<td>Duration of procedure</td>
<td>4-6 hours</td>
<td>2 hours</td>
</tr>
<tr>
<td>Vitals</td>
<td>Q15min</td>
<td>Q30min</td>
</tr>
<tr>
<td>Rescue medications</td>
<td>The following medications will be available to RN: Albuterol, Famotidine, Diphenhydramine, Methylprednisolone, Epinephrine</td>
<td></td>
</tr>
</tbody>
</table>
UPMC PENICILLIN ALLERGY PATHWAY

Successful completion of β-lactam allergy assessment questionnaire

- Denies allergy
- Has since tolerated the β-lactam they report being allergic to
- Side effect (gastrointestinal, headache)
- Family history

Unable to obtain reliable history from patient or family member

Administer penicillins or cephalosporins

Prior penicillin tolerated: administer penicillins or cephalosporins

Prior cephalosporin tolerated: administer same cephalosporin or non-cross-reacting cephalosporin (Table)

REACTION

Very Low Risk
- Patient does not remember details
- Pruritus without rash
- Pre-syncpe only (after oral dose)

Low Risk
- Minor rash
- Maculopapular rash

Moderate Risk
- Urticaria (hives) ≤ 10 years ago

High Risk
- Anaphylaxis
- Urticaria (hives) less than 10 years ago
- Angioedema or laryngeal edema
- Wheezing
- Shortness of breath
- Syncope
- Hypotension
- Recurrent reactions (upon re-exposure)
- Reactions to multiple β-lactam antibiotics
- No reaction documented and unable to obtain reliable history from patient or family member

Currently pregnant or with unstable asthma, COPD, CHF, MI, arrhythmias, angina

Oral amoxicillin challenge
- OR
Full dose cephalosporin
- OR
Oral/IV graded challenge to penicillins or cross-reacting cephalosporins (Table)
- OR
Full dose non-cross-reacting cephalosporins (Table)

In absence of penicillin skin testing
- Oral/IV graded challenge to penicillins or cross-reacting cephalosporins (Table)
- OR
Full dose non-cross-reacting cephalosporins (Table)

Penicillin skin testing followed by oral/IV graded challenge (preferred)

In absence of penicillin skin testing
- Oral/IV graded challenge to non-cross-reacting cephalosporins (Table)
- OR
Desensitization to penicillins or cross-reacting cephalosporins

Avoid β-lactam
Consult Infectious Diseases and Allergy if β-lactam therapy necessary

SEVERE REACTIONS
- Stevens-Johnson syndrome (SJS)
- Toxic epidermal necrolysis (TEN)
- Drug reaction with eosinophilia and systemic symptoms (DRESS)
- Acute generalized exanthematous pustulosis (AGEP)
- Hemolytic anemia
- Nephritis
- Hepatitis
- Serum sickness (fever, joint pain)
- Drug fever
High Risk
- Anaphylaxis
- Urticaria (hives) less than 10 years ago
- Angioedema or laryngeal edema
- Wheezing
- Shortness of breath
- Syncope
- Hypotension
- Recurrent reactions (upon re-exposure)
- Reactions to multiple β-lactam antibiotics
- No reaction documented and unable to obtain reliable history from patient or family member

Yes

Penicillin skin testing followed by oral/IV graded challenge (preferred)

In absence of penicillin skin testing
Oral/IV graded challenge to non-cross-reacting cephalosporins (Table)

OR
Desensitization to penicillins or cross-reacting cephalosporins

SEVERE REACTIONS
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THANK YOU !