

STEWARDSHIP SKILLS TO ASSIST PATIENTS REPORTING ANTIBIOTIC ALLERGIES

June 26, 2024

NC CLASP Hospital Stewardship
Year 2

INTRODUCTIONS

Please put your name, hospital, and location in the chat!

CONFLICT OF INTEREST DISCLOSURES

- ▶ The views and opinions expressed in this series are those of the speakers and do not reflect the official policy or position of any agency of the US or NC government or UNC.
- ▶ None of the speakers or planners have any relevant financial relationships with ineligible companies to disclose.
- ▶ The speakers do not intend to discuss an unapproved/investigative use of a commercial product/device in this series, and all COI have been mitigated.
- ▶ These slides contain materials from a variety of colleagues, as well as the CDC, WHO, AHRQ, etc.

CME AND CE CREDIT



▶ CME & CE for participants

- ▶ Attendance and active participation per learning session
- ▶ Click the link in the chat during the session to document your attendance
- ▶ Complete surveys as requested

TODAY'S DISCUSSION

Scope
& Impact

Assessing Allergy
History

Management
Strategies / Skills

De-labeling

Education, Education, Education

Stewardship skills to assist patients reporting antibiotic allergies

SCOPE AND IMPACT OF ANTIBIOTIC ALLERGY

ADVERSE EVENTS TO ANTIMICROBIALS

▶ **Effects resulting from antibacterial activity:**

- ▶ Gastrointestinal effects on gut microbiome: diarrhea, overgrowth of toxin-producing *Clostridioides difficile*

▶ **Toxicity not-associated with target pharmacology**

- ▶ Aminoglycoside, penicillin, vancomycin, trimethoprim-sulfamethoxazole renal effects
- ▶ Linezolid thrombocytopenia, hepatic effects

▶ **Immunologically mediated effects**

- ▶ Cell-mediated, usually-delayed, hypersensitivity reactions
Delayed beta-lactam rash, abacavir hypersensitivity, >24hours
- ▶ Immediate hypersensitivity reactions, preformed IgE/mast cell mechanism, rare but serious, 0-6 hours
wheezing/coughing, hives/itching, palmar erythema, angioedema, and/or anaphylaxis

▶ **Severe, but largely unpredictable reactions**

- ▶ e.g Steven-Johnson Syndrome, Erythema multiforme, rare vancomycin reactions


PENICILLIN AND BETA-LACTAM ALLERGY EPIDEMIOLOGY

- ▶ ~10% of all U.S. report an allergic reaction to a penicillin-class antibiotic;
> 1% of the population are actually allergic
- ▶ Penicillin /ampicillin/amoxicillin: reactions not uncommon, anaphylaxis is rare
 - ▶ One fatal amoxicillin reaction in UK 1972-2007
- ▶ About 10% of patients lose their **penicillin** allergy each year
 - ▶ After 10 years, 80-90% of true penicillin allergies have resolved
- ▶ Time since reaction is but one factor in assessing risk

PENICILLIN ALLERGIES: IMPACT

- ▶ 10% of all patients report a penicillin allergy
- ▶ Only 10% of allergy reporters are *actually* allergic
- ▶ Penicillin allergy is associated with increased risk of surgical-site infection, MRSA infection, C-diff, and possibly death
- ▶ Alternative antibiotics are often suboptimal:
 - ▶ Broader-spectrum: vancomycin, fluoroquinolones, carbapenems
 - ▶ Less effective: vancomycin, clindamycin, oral cephalosporins
 - ▶ More likely to cause *C. difficile*: carbapenems, 3rd and 4th gen cephalosporins, fluoroquinolones
 - ▶ Patients with history of severe beta-lactam allergies may require *more than one* alternate antibacterial agent to comprise adequate empiric therapy¹

Risk of meticillin resistant *Staphylococcus aureus* and *Clostridium difficile* in patients with a documented penicillin allergy: population based matched cohort study

 OPEN ACCESS

Kimberly G Blumenthal *assistant professor of medicine*^{1,2,3}, Na Lu *biostatistician*¹, Yuqing Zhang *professor of medicine*^{1,3}, Yu Li *research assistant*^{1,2}, Rochelle P Walensky *professor of medicine*^{2,3,4}, Hyon K Choi *professor of medicine*^{1,3}

- ▶ Population study in the UK
- ▶ Penicillin allergy associated with:
 - ▶ MRSA infection: adjusted HR 1.69 (95% CI: 1.51-1.90)
 - ▶ *C. difficile* infection: adjusted HR 1.26 (95% CI: 1.12-1.40)

Patients reporting penicillin allergy were 69% more likely to have an MRSA infection and 26% more likely to have a C-diff infection

BMJ, 2018

The Impact of a Reported Penicillin Allergy on Surgical Site Infection Risk

Kimberly G. Blumenthal,^{1,2,3,4} Erin E. Ryan,^{5,6} Yu Li,^{1,2} Hang Lee,^{4,7} James L. Kuhlen,⁸ and Erica S. Shenoy^{2,4,5,6}

¹Division of Rheumatology, Allergy, and Immunology, Department of Medicine, ²Medical Practice Evaluation Center, and ³Edward P. Lawrence Center for Quality and Safety, Massachusetts General Hospital, Boston, ⁴Harvard Medical School, Boston, ⁵Division of Infectious Disease, Department of Medicine, ⁶Infection Control Unit, and ⁷Biostatistics Center, Massachusetts General Hospital, Boston; and ⁸Acadia Allergy and Immunology, Department of Medicine, University of South Carolina School of Medicine, Greenville, South Carolina

- ▶ Analysis of patients undergoing one of 5 common surgeries at Mass Gen
- ▶ Penicillin allergy: adjusted OR of 1.51 (1.02-2.22) for surgical site infection
 - ▶ Multivariate regression analysis on 8385 pts, 922 reported penicillin allergy, 241 had SSI
 - ▶ Only 12% received cefazolin (92% of penicillin non-allergic received cefazolin)
 - ▶ 49% of penicillin-allergic received clindamycin and 35% received vancomycin

Patients reporting penicillin allergy had 51% higher odds of surgical site infection.

Clinical Infectious Diseases, 2018

Recorded Penicillin Allergy and Risk of Mortality: a Population-Based Matched Cohort Study

*Kimberly G. Blumenthal, MD, MSc^{1,2,3,4}, Na Lu, MPH^{1,5}, Yuqing Zhang, DSc^{1,3,4,5},
Rochelle P. Walensky, MD, MPH^{2,3,4,6}, and Hyon K. Choi, MD, DrPH^{1,3,4}*

- ▶ 63,690 patients with penicillin allergy; 237,167 patients without
- ▶ Median follow-up: 6 years
- ▶ Adjusted hazard ratio for mortality: 1.14 (1.12-1.17)

Patients reporting penicillin allergies were 14% more likely to die

Journal of General Internal Medicine, 2019

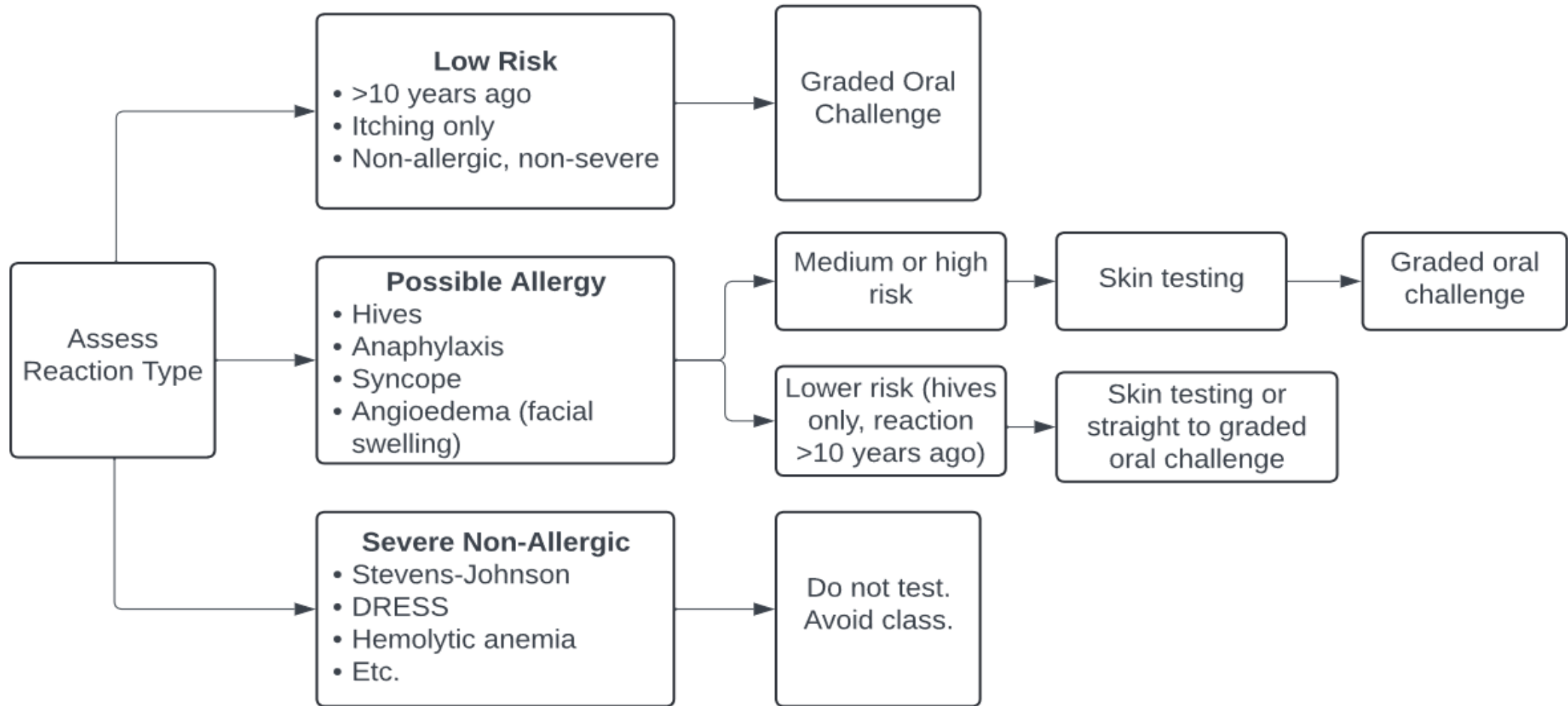
Stewardship skills to assist patients reporting antibiotic allergies

ASSESSING ANTIBIOTIC ALLERGY

KEY HISTORICAL DETAILS

- ▶ When did the patient have the reaction?
 - ▶ How long in the past?
 - ▶ Did the reaction occur following first dose, or after several doses?
- ▶ What was the reaction?
 - ▶ Non-reaction: family history; patient denies history
 - ▶ Intolerance: GI upset, headache, fatigue, etc.
 - ▶ Low-risk: itching alone, rash without hives, flushing/redness
 - ▶ High-risk Allergy: face/lip/tongue swelling, wheezing, shortness of breath, flushing
- ▶ What was the treatment for the reaction?
 - ▶ Was a higher level of care required to care for the patient? (went to ED, transferred to ICU, etc)
- ▶ Has the patient taken that class since then? Similar classes?
 - ▶ Penicillin allergy but tolerated cephalosporins?

EXAMPLE ALGORITHM



PENICILLIN INTOLERANCES: 4 POSSIBILITIES (THESE APPLY TO ANY ANTIBIOTIC)

1. Non-severe, non-allergic
 - ▶ Non-urticarial early-onset rash, GI symptoms only, behavior change, etc.
 - ▶ Unlikely to repeat
2. True allergy, still allergic
3. True allergy, allergy resolved
4. Severe, non-allergic reaction

PATIENT NOT ALLERGIC (~ZERO RISK)

▶ Family history

- ▶ Specific allergies are not familial

▶ Tolerated the penicillin *since* initial reported reaction

- ▶ We often find penicillin-allergic patients who took a full course of a penicillin recently

▶ Intolerance, not allergy (Non-allergic, non-severe)

- ▶ Reaction was GI upset, nausea, vomiting, diarrhea, otherwise unrelated
- ▶ Non-urticarial, early-onset rash in childhood

TRUE ALLERGY: RAPID ONSET REACTION

- ▶ IgE-mediated reaction
- ▶ Onset: <1 hour, up to 6 hours
- ▶ Symptoms: itching, palmar erythema, wheezing, hives, angioedema, and/or anaphylaxis
- ▶ Treatment often required, often with a higher level of care
 - ▶ Antihistamines, beta-agonists for wheezing, epinephrine if anaphylaxis
- ▶ Assessment: If event was very distant in time: Allergy specialist evaluation. Use alternate agent in short term. If absolutely required: e.g syphilis in a pregnant patient, consider de-sensitization.

HIGH RISK: AVOID THE IMPLICATED DRUG FOREVER

- ▶ High-risk reactions are *severe* and are *not classic allergy*
- ▶ Reaction types:
 - ▶ Stevens-Johnson Syndrome (SJS)
 - ▶ Toxic Epidermal Necrolysis (TEN)
 - ▶ Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)
 - ▶ Now called Drug-Induced Hypersensitivity Syndrome (DIHS)
 - ▶ Serum Sickness
 - ▶ Hemolytic anemia
 - ▶ Acute Interstitial nephritis
- ▶ OK to use beta-lactams that were previously tolerated. Never give the offending agent; generally avoid all that class of drug (eg beta-lactams) that are not *known* to be tolerated

ASSESSING B-LACTAM CROSS REACTIVITY

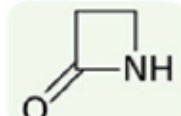
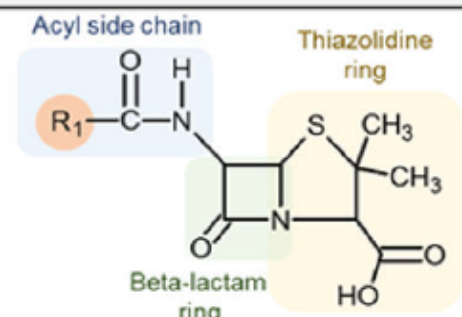
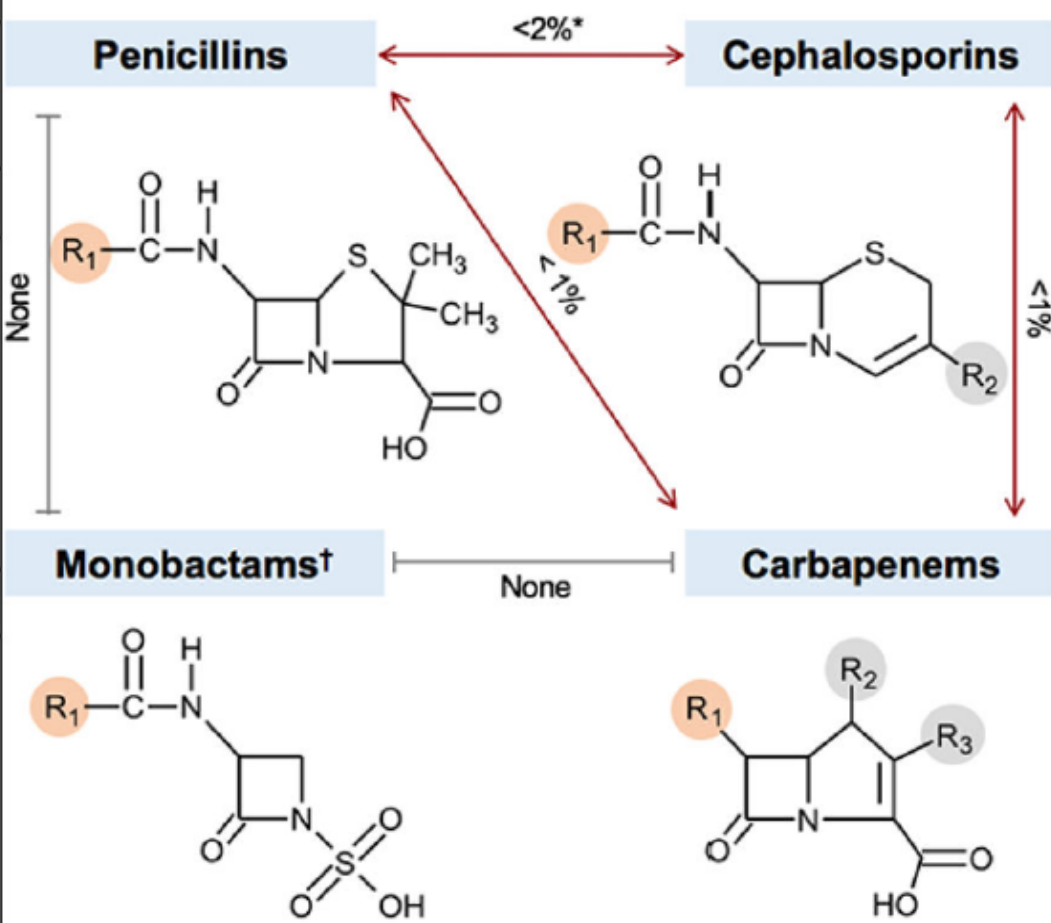
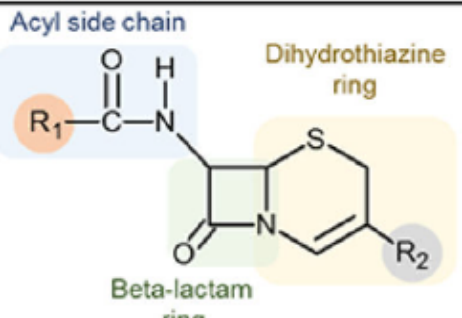
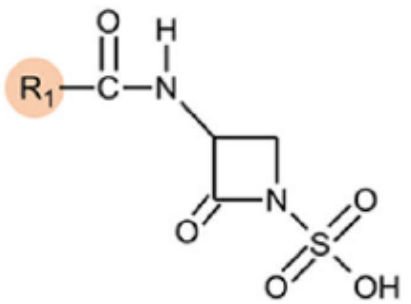
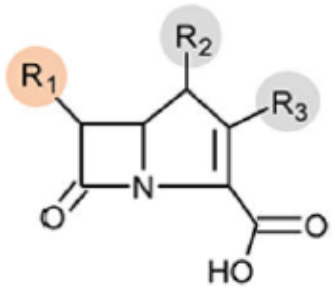
| Basic structures | Beta-Lactam structures and rates of cross-reactivity | Clinically relevant cross-reactivity |
|--|---|---|
| Beta-lactam ring | | |
|  | | |
| Penicillin structure | | Similar side chains, Penicillins (R1) |
|  |  <p>None</p> <p>None</p> | <ul style="list-style-type: none"> • Penicillin VK & penicillin G |
| Cephalosporin structure | | Shared side chains, Penicillins & cephalosporins (R1) |
|  | | <ul style="list-style-type: none"> • Amoxicillin[^] & cefadroxil, cefprozil, cefatrizine • Ampicillin[^] & cefaclor, cephalixin, cephadrine, cephaloglycine |
| | Monobactams [†] | Shared side chains, Cephalosporins (R1) |
| |  | <ul style="list-style-type: none"> • Cefaclor, cephalixin |
| | Carbapenems | <ul style="list-style-type: none"> • Cefepime, ceftriaxone, cefotaxime, cefpodoxime, ceftizoxime • Ceftazidime and aztreonam |
| |  | No shared side chains, Penicillins & cephalosporins (R1) |
| | | <ul style="list-style-type: none"> • Cefazolin |

FIGURE 1: BETA-LACTAMS THAT SHARE IDENTICAL OR SIMILAR R1 AND IDENTICAL R2 SIDE CHAINS

Key: R1 = Identical R1 side chain; R1* = similar side chain; R2 = Identical R2 side chain

| | Penicillin G | Penicillin VK | Amoxicillin | Ampicillin | Nafcillin/Oxacillin | Piperacillin-Tazobactam | Cefazolin | Cephalexin | Cefadroxil | Cefuroxime | Cefoxitin | Cefdinir | Cefpodoxime | Ceftriaxone | Cefotaxime | Ceftazidime | Cefepime | Ceftaroline | Ceftolozane-Tazobactam | Aztreonam |
|-------------------------|--------------|---------------|-------------|------------|---------------------|-------------------------|-----------|------------|------------|------------|-----------|----------|-------------|-------------|------------|-------------|----------|-------------|------------------------|-----------|
| Penicillin G | | R1* | | | | | | | | | | | | | | | | | | |
| Penicillin VK | R1* | | | | | | | | | | | | | | | | | | | |
| Amoxicillin | | | | R1* | | | | R1* | R1 | | | | | | | | | | | |
| Ampicillin | | | R1* | | | | | R1 | R1* | | | | | | | | | | | |
| Nafcillin/Oxacillin | | | | | | | | | | | | | | | | | | | | |
| Piperacillin-Tazobactam | | | | | | | | | | | | | | | | | | | | |
| Cefazolin | | | | | | | | | | | | | | | | | | | | |
| Cephalexin | | | R1* | R1 | | | | | R1* | | | | | | | | | | | |
| Cefadroxil | | | R1 | R1* | | | | R1* | | | | | | | | | | | | |
| Cefuroxime | | | | | | | | | | | | | | | | | | | | |

Stewardship skills to assist patients reporting antibiotic allergies

ANTIBIOTIC ALLERGY MANAGEMENT SKILLS AND INTERVENTIONS

INPATIENT STRATEGIES FOR STEWARDSHIP

- ▶ Closely examine how allergies are documented
 - ▶ When
 - ▶ By whom: (it's not primarily MDs, Pas, RNs)
 - ▶ EMR details
- ▶ Train those who actually take histories
- ▶ Learn / teach EMR searching for previously-tolerated agents
- ▶ Refer for allergy testing
- ▶ Educate clinicians at all levels
- ▶ Educate patients

RECORDING ALLERGIES – ENGINEERING THE LABEL



Review EMR recording algorithm

Include required entries for key fields

Reaction

Timing of reaction after administration

How long ago was the reaction?

Include a free text box and encourage its use



Educate those who actually take
and record allergy histories

EMT, nursing assistants

RNs

Providers

Pharmacists

SEARCHING THE PATIENT'S DRUG HISTORY



Allergy labels persist, prior administration of specific antibiotics is often forgotten



Clinicians will search/read the past *progress notes* to learn if the patient has received an antibiotic safely.



Use the EMR to search the actual drug history for antibiotics previously given.

Beware of one-time entries that suggest order was discontinued before the drug was administered.

De-sensitized?

EPIC EXAMPLE

- ▶ Patient reports penicillin allergy in 2012. Has penicillin-susceptible infection, started on meropenem at outside hospital.
- ▶ Can they take cephalosporins?
- ▶ Step 1: Go to Chart Review, Medications
 - ▶ Apply Antibiotics Filter

Filters Current Meds Only Abx Anticoag A

| | |
|----------------------|---|
| Department Specialty | Medication |
| Encounter Department | Pharmaceutical Class |
| Encounter | Prescribing Provider |
| Episode | Schedule Level |
| Generic Drug Name | <input checked="" type="checkbox"/> Therapeutic Class |

Include **Exclude** Therapeutic Class contains... +

| Therapeutic Class | Count | Last Date |
|--|-------|-----------|
| <input type="checkbox"/> ANALGESICS | 4 | |
| <input type="checkbox"/> ANESTHETICS | 4 | |
| <input type="checkbox"/> ANTIARTHRITICS | 2 | |
| <input checked="" type="checkbox"/> ANTIBIOTICS | 6 | |
| <input type="checkbox"/> ANTIHISTAMINES | 2 | |
| <input type="checkbox"/> ANTIVIRALS | 1 | |
| <input type="checkbox"/> CNS DRUGS | 8 | |
| <input type="checkbox"/> COUGH/COLD PREPARATI... | 2 | |
| <input type="checkbox"/> ELECT/CALORIC/H2O | 4 | |
| <input type="checkbox"/> GASTROINTESTINAL | 8 | |
| <input type="checkbox"/> HORMONES | 1 | |
| <input type="checkbox"/> PSYCHOTHERAPEUTIC DR... | 17 | |
| <input type="checkbox"/> SEDATIVE/HYPNOTICS | 1 | |
| <input type="checkbox"/> SKIN PREPS | 2 | |
| <input type="checkbox"/> VITAMINS | 5 | |

EPIC EXAMPLE

| | | |
|-----|---|--|
| IP | | meropenem (MERREM) 1 g in sodium ... |
| IP | ✘ | clindamycin (CLEOCIN) 18 mg/mL inje... |
| AMB | ✘ | ofloxacin (OCUFLOX) 0.3 % ophthalmi... |
| | | ofloxacin (OCUFLOX) 0.3 % o |
| AMB | ✘ | azithromycin (ZITHROMAX) 200 mg/5... |
| AMB | | cefdinir (OMNICEF) 250 mg/5 mL sus... |
| AMB | ✘ | azithromycin (ZITHROMAX) 200 mg/5... |

▶ Step 2: Review antibiotic history

- ▶ Patient took cefdinir in 2016!
 - ▶ Patient reports no problem with that
-
- ▶ Almost certainly will tolerate cephalosporin now

COMMENTS ON DESENSITIZATION

- ▶ If medication allergies are handled optimally, desensitization will be an infrequent event
- ▶ It only prevents IgE-mediated reactions!!!
- ▶ Deceptively easy solution to prescribe (though not so easy for the pharmacy)
- ▶ It can delay timely therapy
 - ▶ Even if successful, full dose not given for hours
 - ▶ Delay may occur as patient's may be required to move to a different unit
- ▶ Gaps in therapy may precipitate allergic reactions
- ▶ For consistency and timely implementation when actually needed, it's best to have order sets pre-built in collaboration with allergy and infectious disease expert clinicians.
- ▶ Oral route can be effective (e.g. CDC STD Guidelines 2021)

Stewardship skills to assist patients reporting antibiotic allergies

DE-LABELING ALLERGIES

DE-LABELING ALLERGY

- ▶ It's easy to think about *primum non nocere*: first do no harm
- ▶ False allergy labels *cause* harm: removal is important yet difficult
- ▶ It's a “reverse diagnosis”
- ▶ Careful history taking
- ▶ Allergy consult if necessary for future antibiotic courses

- ▶ Educate, Educate, Educate
Healthcare workers *and* patients

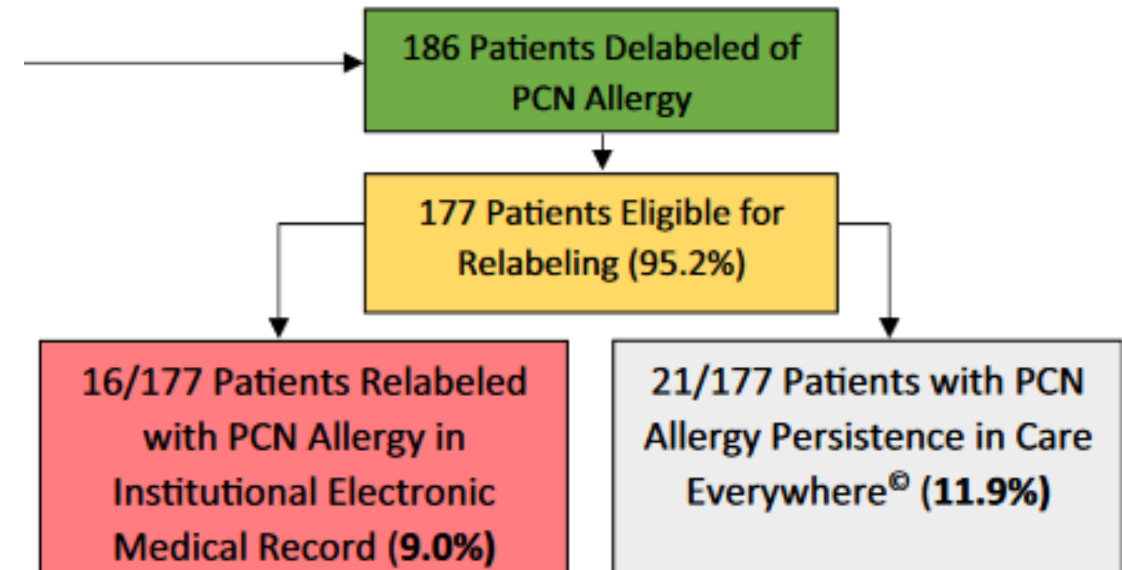
VERIFYING ALLERGY

- ▶ Determine if patient is currently truly allergic
 - ▶ As opposed to non-allergic intolerance or resolved allergy
- ▶ Limitations: These tools *cannot* detect non-IgE mediated reactions
 - ▶ Serum sickness, Stevens-Johnson, DRESS, drug-induced liver injury, etc.
- ▶ Skin testing:
 - ▶ Scratch or prick testing, followed by intradermal injection
 - ▶ Commercially available penicillin allergens; also can use specially prepared penicillin G
- ▶ Graded oral challenge:
 - ▶ Used if considered low-risk scenario (>10 years ago or probably not an allergic reaction)
 - ▶ Take 10% of dose under close observation. If tolerated → take full dose under observation

ALLERGY LABELS

“Sticky penicillin allergy labels”

- ▶ Patients are tested, educated and delabeled
- ▶ Allergy labels may persist in other EHRs
- ▶ Patients may continue to report penicillin allergy



Olds G and Chow T, *Ann Allergy Asthma Immunol* 2024

CHALLENGES – THEY CAN BE OVERCOME

- ▶ Antibiotic intolerances are not uncommon
 - ▶ β -lactam allergies are among the most common drug reactions, and can be serious
- ▶ "Allergy" labels are used for various intolerances
- ▶ Clinicians reasonably fear overriding or removing a documented allergy
 - ▶ Pretty sure it's not a true allergy vs risk of anaphylaxis
- ▶ Improving allergy documentation can improve patient care (and safety).
- ▶ Drug allergy (real or perceived) makes patients and those who care for them feel uncomfortable – even when there is no reaction to the medication!
- ▶ Systems and tools to optimize management of patients reporting antibiotic allergies can make for better care and enhanced stewardship!

NC CLASP HOSPITAL SESSION OVERVIEW

NC CLASP - YEAR ONE

CDC 2019

Core Elements of Hospital Antimicrobial Stewardship Programs

Core Elements of Hospital Antibiotic Stewardship Programs



Hospital Leadership Commitment

Dedicate necessary human, financial, and information technology resources.



Accountability

Appoint a leader or co-leaders, such as a physician and pharmacist, responsible for program management and outcomes.



Pharmacy Expertise (previously “Drug Expertise”):

Appoint a pharmacist, ideally as the co-leader of the stewardship program, to help lead implementation efforts to improve antibiotic use.



Action

Implement interventions, such as prospective audit and feedback or preauthorization, to improve antibiotic use.



Tracking

Monitor antibiotic prescribing, impact of interventions, and other important outcomes, like *C. difficile* infections and resistance patterns.



Reporting

Regularly report information on antibiotic use and resistance to prescribers, pharmacists, nurses, and hospital leadership.



Education

Educate prescribers, pharmacists, nurses, and patients about adverse reactions from antibiotics, antibiotic resistance, and optimal prescribing.

NC CLASP: YEAR TWO

6 hour-long learning sessions
September 2023-May/July 2024

CE included: CME, RN,
Pharmacist (ACPE)

Two in-person conferences

- ▶ Discussion topics have included:
- ▶ Diagnostic stewardship/ collaborating with the Clinical Microbiology lab
- ▶ Stewardship in skin/skin structure infections
- ▶ Impacting empiric therapy decisions
- ▶ **Handling antibiotic allergies**
- ▶ Stewardship in transitions of care to and from the Emergency Department
- ▶ May 22, 2024: Full day, in-person conference
- ▶ Regional in-person sessions: February, April, July

BREAK OUT OR GROUP DISCUSSION

- ▶ Questions?
- ▶ Comments?
- ▶ Discussion?

- ▶ Feedback on NC CLASP program?

BIBLIOGRAPHY: ANTIBIOTIC ALLERGIES

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- ▶ Stone, et al. The Challenge of De-labeling Penicillin Allergy. Allergy. 2020;75: 273–288

THE NORTH CAROLINA CLINICAL ANTIBIOTIC STEWARDSHIP PARTNERS (NC CLASP)

- ▶ All the information from today's session will be on our website <https://spice.unc.edu/ncclasp/>



THANK YOU!!



North Carolina
Clinical Antibiotic
Stewardship Partners