Drug Allergy Practice Parameter:
Implementation of Key Recommendations

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Allergy & Immunology Program Director

Disclosures

- No relevant disclosures
Drug Allergy Parameter Update

- Last parameter published 2010
- Next parameter will update ~ 14 sections
- Currently in draft status
- No final recommendations have been made
  - All recommendations in this presentation should be considered as preliminary
- Expected publication in 2022
Updates to Drug Allergy Parameter

- **Diagnostic Tests**
  - Drug challenge procedures
  - Delayed reaction testing
  - Pharmacogenomics
- **Other Updates**
  - NSAID Hypersensitivity
  - Chemotherapeutics
  - Biologics
  - Excipients
- **Antibiotic Updates**
  - Penicillins
  - Cephalosporins
  - Carbapenems
  - Monobactams
  - Sulfonamides
  - Fluoroquinolones
  - Macrolides

Topics to Cover

- **Diagnostic Tests**
  - Drug challenge procedures
  - Delayed reaction testing
  - Pharmacogenomics
- **Other Updates**
  - **NSAID Hypersensitivity**
    - Aspirin challenge for acute cardiovascular disease
  - Chemotherapeutics
  - Biologics
  - Excipients
- **Antibiotic Updates**
  - Penicillins
  - Cephalosporins
  - Carbapenems
  - Monobactams
  - Sulfonamides
  - Fluoroquinolones
  - Macrolides
Drug Challenge Considerations

- Drug challenges are typically indicated in patients who after evaluation are deemed unlikely to be allergic to the drug
- Shared decision making may be used in patients with a higher pretest probability of true allergy or a history of more severe reactions when the benefit of drug therapy outweighs the risks
Severe Cutaneous Adverse Drug Reactions | Severe Drug Anaphylaxis*
---|---
SJS/TEN | Organ Specific Drug Reactions
DRESS | Cytopenias (anemia, neutropenia, leukopenia, thrombocytopenia)
AGEP | Drug induced liver injury
Drug-Induced Neutrophilic Dermatosis | Nephritis
Sweet's syndrome | Pneumonitis
Meningitis | 
Drug-Induced Autoimmune Diseases | Pancreatitis
Bullous pemphigoid | 
Pemphigus vulgaris | Drug Induced Vasculitis
Linear IgA bullous disease | Leukocytoclastic vasculitis
Drug induced lupus | Eosinophilic granulomatosis with polyangiitis
Drug-induced lupus | 
Other Cutaneous Drug Reactions | 
Generalized bullous fixed drug eruption | 
Exfoliative dermatitis | 

1 or 2 step Challenge Preferred

<table>
<thead>
<tr>
<th>Consensus Based Statement</th>
<th>Strength of Recommendation</th>
<th>Certainty of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>We suggest that when the clinical probability of a drug allergy is low, in patients without contraindications for a drug challenge, that it be performed with a 1- or 2-step drug challenge.</td>
<td>Conditional</td>
<td>Low</td>
</tr>
</tbody>
</table>
Open Drug Challenge Protocols for Immediate Reactions

<table>
<thead>
<tr>
<th>Step</th>
<th>Dose†</th>
<th>Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-Step</td>
<td>1 tab or Full PO/IV /IM/SC dose*</td>
<td>30-60 min</td>
</tr>
<tr>
<td>2-Step</td>
<td>Step 1:¼ tab PO or 1/10th IV/IM/SC dose</td>
<td>30-60 min</td>
</tr>
<tr>
<td></td>
<td>Step 2: 1 tab or Full PO/IV /IM/SC dose*</td>
<td>30-60 min</td>
</tr>
</tbody>
</table>

Criteria for positive reaction: Urticaria, angioedema, exanthem, wheezing, hypoxia, hypotension, anaphylaxis.

Criteria for possible reaction***: Flushing, vomiting, cough, abdominal cramping, persistent pruritus without rash, fever, mouth or eye soreness.

Doubtful reactions***: Dizziness, tachycardia, subjective lip/tongue swelling, subjective throat tightness, lump in throat, dyspnea, transient pruritus without rash, headache.

†Comparably dosed oral solution may be used (1/10th or full dose).
*For very low risk patients without significant comorbidities, may use single full dose challenge (e.g. Sulfonamide & Penicillin)
**For mild exanthems, may use single full dose challenge
***Consider placebo-controlled challenges for possible or doubtful reactions to confirm or refute allergy.

Original Article

**Differentiating Between β-Lactam-Induced Serum sickness-Like Reactions and Viral Exanthem in Children Using a Graded Oral Challenge**

Luca Dell’Orco, BSc (h.c.), Silvane Gabrielli, MSc, Elisa M. Abrams, MD, FRCP(c), Andrew O’Keefe, MD, Jennifer L. Pretorius, PhD, FAAC, Elana Levine, MD, MG, Tracey Phir, MD, MG, Adele Atkinson, MD, FRCP(c), Thomas Elvey, MD, Christine McCouler, MSc, and Moshe Ben-Shouah, MD, MSc

Table 1. Demographic and initial reaction information collected at clinic visit

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients (n = 75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at index reaction, median (IQR)</td>
<td>2.00 (1.0, 4.00)</td>
</tr>
<tr>
<td>Sex, n (% males)</td>
<td>35 (46.7)</td>
</tr>
<tr>
<td>Symptoms of β-lactam reaction</td>
<td></td>
</tr>
<tr>
<td>Pruritus (generalized)</td>
<td>315 (41.3)</td>
</tr>
<tr>
<td>Urticaria</td>
<td>48 (65.3)</td>
</tr>
<tr>
<td>Angioedema</td>
<td>26 (34.7)</td>
</tr>
<tr>
<td>Macular/regular rash</td>
<td>33 (44.0)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>8 (10.7)</td>
</tr>
<tr>
<td>Throat tightness</td>
<td>2 (2.7)</td>
</tr>
<tr>
<td>Breathing difficulties</td>
<td>3 (4.0)</td>
</tr>
<tr>
<td>Arthritis/myalgia</td>
<td>75 (100)</td>
</tr>
<tr>
<td>Fever</td>
<td>30 (40.0)</td>
</tr>
</tbody>
</table>

**Challenge:**
10% dose then 20 min later 90% dose
Challenges may be considered for SSLR, however 25% may have benign symptoms with subsequent course

Placebo Challenges for Subjective Reactions or Multiple Drug Intolerance

<table>
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<tr>
<th>Consensus Based Statement</th>
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<tbody>
<tr>
<td>We suggest that placebo-controlled drug challenges be considered in patients with a history of primarily subjective symptoms and/or multiple reported drug allergies.</td>
<td>Conditional</td>
<td>Low</td>
</tr>
</tbody>
</table>
12% of nocebo reactions were objective

137/228 (60%) had reactions to placebo

Penicillin Allergy Updates

Role of Skin Testing
Role of Direct Challenge
Why Penicillin Allergy Labels Matter

Figure 4. Health Implications and Burden of the Penicillin-Allergy Label.

Castells MC, Khan DA, Phillips EC. NEJM 2019;381:2338-51

Original Article

The Effect of Penicillin Allergy Testing on Future Health Care Utilization: A Matched Cohort Study

Eric Macy, MD, MS, and Yu-Hsiang Shu, MS, PhD, San Diego and Pasadena, Calif

Delabeling led to cost reduction of $1915 per patient per year

Consensus Based Statement

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</thead>
<tbody>
<tr>
<td>We recommend that a proactive effort should be made to delabel a penicillin allergy, if appropriate.</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

Methods to Delabel Penicillin Allergy

<table>
<thead>
<tr>
<th>Setting</th>
<th>Method</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outpatient</td>
<td>Referral based skin test and challenge</td>
<td>With or without minor determinant mixture</td>
</tr>
<tr>
<td></td>
<td>Direct challenge</td>
<td>Low risk histories</td>
</tr>
<tr>
<td></td>
<td>Protocol driven</td>
<td>Allergy clinic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Other clinics</td>
</tr>
<tr>
<td>Inpatient</td>
<td>Allergy consultation</td>
<td>Least efficient</td>
</tr>
<tr>
<td></td>
<td>Proactive testing protocol</td>
<td>Pharmacists or other healthcare providers</td>
</tr>
<tr>
<td></td>
<td>Intensive care unit testing</td>
<td>Skin testing</td>
</tr>
<tr>
<td></td>
<td>Emergency Department</td>
<td>Skin testing or direct challenge by non-allergy specialists or other healthcare providers</td>
</tr>
</tbody>
</table>

No Need to Challenge Patients with Invalid Histories of Penicillin Allergy

<table>
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</thead>
<tbody>
<tr>
<td>We recommend against testing in patients with a history inconsistent with penicillin allergy (such as headache or family history of penicillin allergy), but a 1-step amoxicillin challenge may be offered to patients who are anxious or request additional reassurance to accept the removal of a penicillin allergy label.</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

When Should Penicillin Skin Tests Be Performed?

<table>
<thead>
<tr>
<th>Consensus Based Statement</th>
<th>Strength of Recommendation</th>
<th>Certainty of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>We suggest penicillin skin testing for patients with a history of anaphylaxis or a recent reaction suspected to be IgE mediated.</td>
<td>Conditional</td>
<td>Low</td>
</tr>
</tbody>
</table>
Are Penicillin Skin Tests Even Needed?

Role of Direct Challenge

Are Penicillin Skin Tests Needed in Children?

Challenge Protocol: 10% dose then 20 min later 90% dose amoxicillin

All immediate and delayed reactions were mild (few cases of SSL reactions)
Consensus Based Statement

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<th>Certainty of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>We recommend against penicillin skin testing prior to direct amoxicillin challenge in pediatric patients with a history of benign cutaneous reaction (such as maculopapular rashes and urticaria).</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

Eligible for RCT: benign cutaneous only reactions
Age 5-17: reaction > 1 yr ago
Age ≥18: reaction > 10 yrs ago

3 reactions with challenge: benign rashes treated with antihistamines


Consensus Based Statement

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</thead>
<tbody>
<tr>
<td>We suggest that direct amoxicillin challenge be considered in adults with distant and benign cutaneous reaction histories (such as maculopapular rashes and urticaria).</td>
<td>Conditional</td>
<td>Low</td>
</tr>
</tbody>
</table>
Are Extended Multiday Penicillin Challenges Necessary?

- European studies
  - Oral challenges 3-10 days
  - Delayed reactions 5-12%
  - Most self-reported, almost all mild and easily treated
- US Studies
  - Full therapeutic courses after negative tests
  - Delayed reactions 0-1.8%

Delayed reactions occurred **6 hrs to 7 days** from initial challenge

No washout: 2/13 reactions with prolonged DC
1 week washout: 1/119 reactions with prolonged DC


Prolonged Penicillin Challenges
Not Needed

<table>
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<th>Certainty of Evidence</th>
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</thead>
<tbody>
<tr>
<td>We recommend against the routine use of prolonged (multi-day) challenges in the evaluation of penicillin allergy.</td>
<td>Strong</td>
<td>Low</td>
</tr>
</tbody>
</table>
Penicillin Allergy & Cross-Reactivity with Other Beta-Lactams

Cephalosporin Allergy is Largely Based on R1 Side Chain

- **Group 1**: Ceftriaxone, Cefotaxime, Cefepime, Cefpodoxime, Cefditoren (may cross-react with Groups 2&3)
- **Group 2**: Cefuroxime (may cross-react with groups 1&3)
- **Group 3**: Ceftazidime, aztreonam (may cross-react with groups 2&3)

1st Generation Cephalosporin Allergy and Aminopenicillin Structural Similarities

Group 4

- ampicillin
- cefaclor
- cephalexin

Group 5

- amoxicillin
- cefadroxil
- cefprozil


Caveats of systematic review

- Almost all patients had confirmed aminopenicillin allergy (not penicillin allergy)
- 89% studies from Europe (11% Canada)

If proven allergy to ampicillin:
risk of positive skin test to 1st/2nd gen aminopenicillin is 16%

risk of positive skin test to unrelated 2nd-4th generation is 2%


Original Article

Tolerability of Cefazolin and Ceftibuten in Patients with IgE-Mediated Aminopenicillin Allergy

Antonino Romano, MD, Rocco Luigi Valluzzi, MD, Cristiano Canuso, MD, Alessandra Zaffiro, MD, Donato Quarantino, MD, and Francesco Gaeta, MD, PhD

Catania, Vatican City, and Rome, Italy

- 131 subjects
  - 98.5% aminopenicillin allergy, 78% with anaphylaxis
- 130/131 had negative cefazolin/ceftibuten skin tests
  - 1 subject (outlier) had positive skin tests to all PCN reagents, cephalosporins and carbapenems
- 129/130 agreed to cefazolin/ceftibuten challenges
  - All 129 had negative challenges


Cefazolin and ceftibuten R1 groups disparate from aminopenicillins
Use of Cephalosporins in Penicillin Allergy

<table>
<thead>
<tr>
<th>Study (reference)</th>
<th>Patients, n</th>
<th>Penicillin reagents</th>
<th>Tested cephalosporin(s)</th>
<th>Positive patients, n (%)</th>
<th>Positive patients, n (in positives)</th>
<th>Administered cephalosporin(s)</th>
<th>Administration route</th>
<th>Reactions, n/Challenges, (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ausina et al.</td>
<td>34 PPL, MDM, AM, AX</td>
<td>Cefadroxil, cefazolin, cefotaxime</td>
<td>5 (14.7)</td>
<td>Cefadroxil (5)</td>
<td>Cefalazolin, cefazolin</td>
<td>Oral, intravenous</td>
<td>0/29</td>
<td>0/30</td>
</tr>
<tr>
<td>Novalbos et al.</td>
<td>41 PPL, MDM, BP, AX</td>
<td>Cefazolin, cefuroxime, ceftriaxone</td>
<td>0 None</td>
<td>Cefalazolin, cefuroxime, ceftriaxone</td>
<td>Intramuscular, intramuscular</td>
<td>0/41</td>
<td>0/41</td>
<td></td>
</tr>
<tr>
<td>Romano et al.</td>
<td>128 PPL, MDM, BP, AM, AX</td>
<td>Cefalotin, cefamandole, cefuroxime, cefazolin, ceftriaxime</td>
<td>14 (10.9)</td>
<td>Cefamandole (9), cefalazolin (8), ceftriaxime (3), cefamandole (2), cefuroxime (2)</td>
<td>Oral, intramuscular</td>
<td>0/101</td>
<td>0/101</td>
<td></td>
</tr>
<tr>
<td>Caimmi et al.</td>
<td>69 PPL, MDM, BP, AX</td>
<td>Cefuroxime</td>
<td>0 None</td>
<td>Cefuroxime azetil</td>
<td>Oral</td>
<td>2/69 (2.9)</td>
<td>0/41</td>
<td></td>
</tr>
<tr>
<td>Romano et al.</td>
<td>252 PPL/BP-OL, MDM/MD, BP, AM, AX, PP</td>
<td>Cefalotin, cefuroxime, cefazolin, cefamandole, cefuroxime, cefazolin, ceftriaxime, cefotaxime, cefepime</td>
<td>14 (33.3)</td>
<td>Cefadroxil (6), cefalor (38), cefalotin (33), cefamandole (11), ceftriaxime (6), cefotaxime (3), cefuroxime (2)</td>
<td>Oral, oral, intramuscular</td>
<td>3/170 (1.8)</td>
<td>0/244</td>
<td></td>
</tr>
<tr>
<td>Al-Ahmad and Rodriguez-Bouza</td>
<td>29 PPL/BP-OL, MDM/MD, BP, AM, AX</td>
<td>Cefuroxime</td>
<td>1 (3.4)</td>
<td>Cefuroxime</td>
<td>Intramuscular</td>
<td>2/28 (7.1)</td>
<td>0/244</td>
<td></td>
</tr>
<tr>
<td>Present study</td>
<td>131 BP-OL, MDM, BP, AM, AX, PP</td>
<td>Cefuroxime, cefibuten</td>
<td>0 (0.7)</td>
<td>Cefalotin (1), cefibuten (1)</td>
<td>Intramuscular, oral</td>
<td>0/129</td>
<td>0/28</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>684</td>
<td></td>
<td>105 (15.4)</td>
<td></td>
<td></td>
<td></td>
<td>13/1564 (0.7)</td>
<td></td>
</tr>
</tbody>
</table>

*AM, Ampicillin; AA, amoxicillin; BP, benzylpenicillin; MD, minor determinant; MDM, minor determinant mixture; PP, piperacillin; PPL, benzylpenicillin-poly-L-lysine.
*Patients with positive skin test results to at least 1 cephalosporin.

(C) Consensus Based Statement

We suggest that for patients with an **unverified non-anaphylactic penicillin allergy**, a cephalosporin can be administered without testing or additional precautions.

<table>
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</thead>
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<tr>
<td>We suggest that for patients with an <strong>unverified non-anaphylactic penicillin allergy</strong>, a cephalosporin can be administered without testing or additional precautions.</td>
<td>Conditional</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

| We suggest that for patients with a history of **anaphylaxis to penicillin**, a non-cross–reactive cephalosporin can be administered without prior testing. | Conditional | Moderate |
In proven penicillin allergy
risk of reacting to carbapenem < 1%


Use of Carbapenems in Penicillin or Cephalosporin Allergy

<table>
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<th>Certainty of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>We recommend that in patients with a history of penicillin or cephalosporin allergy, a carbapenem may be administered without testing or additional precautions.</td>
<td>Strong</td>
<td>Moderate</td>
</tr>
</tbody>
</table>
Cephalosporin Quinolone & Macrolide Allergy

Cephalosporin Cross-Reactivity

- Most data suggest that at least 90% of cephalosporin allergy is due to R1 side chain
- Cephalosporin allergic patients typically tolerate other cephalosporins with disparate R1 side chains, especially if skin test negative
  - 102 cephalosporin allergic patients tolerated 326 challenges to skin test negative cephalosporins

### Alternative Cephalosporins with History of Cephalosporin Allergy

<table>
<thead>
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</tr>
</thead>
<tbody>
<tr>
<td>We suggest that for patients with a history of non-anaphylactic cephalosporin allergy, direct challenges (without prior skin test) to cephalosporins with dissimilar side chains be performed to determine tolerance.</td>
<td>Conditional</td>
<td>Moderate</td>
</tr>
<tr>
<td>We suggest that for patients with a history of anaphylaxis to a cephalosporin, a negative cephalosporin skin test should be confirmed prior to administration of a parenteral cephalosporin with a non-identical R1 side chain.</td>
<td>Conditional</td>
<td>Low</td>
</tr>
</tbody>
</table>

### Penicillin Administration with History of Cephalosporin Allergy

<table>
<thead>
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</thead>
<tbody>
<tr>
<td>We suggest against penicillin skin testing in patients with a non-anaphylactic history to cephalosporins prior to administration of penicillin therapy.</td>
<td>Conditional</td>
<td>Low</td>
</tr>
<tr>
<td>We suggest that in patients with a history of anaphylaxis to cephalosporins, penicillin skin testing and drug challenge should be performed prior to administration of penicillin therapy.</td>
<td>Conditional</td>
<td>Low</td>
</tr>
</tbody>
</table>
Quinolone Allergy

- Incidence of IgE-mediated quinolone allergy is increasing
- First dose reactions due to MRGPRX2
- Delayed reactions to quinolones occur in 2-3%
- Skin testing not reliable due to high irritant potential of quinolones
- Drug challenges recommended for diagnosis
- No clear patterns of cross-reactivity


Confirmed hypersensitivity
- History of anaphylaxis to moxifloxacin, OR=96
- Ciprofloxacin is culprit, OR=0.11
- Prick tests positive to culprit
  - 7/7 moxifloxacin
  - 3/18 ciprofloxacin
- BAT + 89.5% HSR cases
- Tolerance to alternative
  - 2/5 ciprofloxacin HSR tolerated levofloxacin
  - 3/5 levofloxacin HSR tolerated ciprofloxacin
  - 3/8 moxifloxacin HSR tolerated ciprofloxacin
  - 2/2 tolerated levofloxacin

Macrolide Allergy

- Relatively uncommon
- Skin testing generally unreliable
- Majority of patients are tolerant upon drug challenge
- Immediate and delayed reactions have been reported
- Anaphylaxis is rare
- Patterns of cross-reactivity amongst macrolides variable

Kuruvilla M. In Drug Allergy Testing. Ed Khan DA, Banerji A 2017

Diagnosis of Macrolide and Quinolone Allergy

<table>
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<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>We suggest using a 1- or 2-step drug challenge without preceding skin testing to confirm tolerance in patients with a history of non-anaphylactic reactions to fluoroquinolones or macrolides.</td>
<td>Conditional</td>
<td>Low</td>
</tr>
</tbody>
</table>
Sulfonamide Allergy

- Sulfonamide allergy is the 2nd most common listed antibiotic allergy
- Allergists have typically avoided challenges due to concerns for severe reactions
- Numerous “desensitization” procedures have been suggested, but prior studies (in HIV patients) show similar effectiveness to drug challenge
- Few data on non-HIV patients

If unidentified “sulfa” allergy: 98.9% had negative challenge
More remote Sulfonamide Reactions More Likely to Pass Challenge

![Graph showing the probability of a challenge failure over latency (years)]

Diagnosis of Sulfonamide Allergy

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>We suggest that for patients with histories of benign cutaneous reactions (e.g. maculopapular exanthem, urticaria) to sulfonamide antibiotics that occurred &gt; 5 years ago, a full dose challenge with trimethoprim-sulfamethoxazole be performed when there is a need to delabel a sulfonamide antibiotic allergy.</td>
<td>Conditional</td>
<td>Low</td>
</tr>
</tbody>
</table>
Aspirin Allergy and Acute Coronary Syndrome

Urgent Need for Aspirin after Coronary Stent

- Many studies have performed “aspirin desensitizations” in patients with histories of both cutaneous and respiratory reactions to aspirin, all with similar high rate of success (>80%)
- Patients in these studies never had confirmatory challenges to determine if truly allergic to aspirin
- Whether these protocols truly induce drug tolerance or are simply a multi-stepped graded challenge is unclear

Aspirin Challenge for Acute Cardiac Needs

- Does patient have asthma that is worsened by ASA/NSAIDs (AERD)?
  - Yes: Premedicate with montelukast, ICS/LABA, prednisone
  - No: Administer 40.5 mg aspirin
    - 90 min
    - Administer 40.5 mg aspirin
    - Observe 90 min & no reaction: ok to take 81 mg aspirin


Simplified Aspirin Challenge for Acute Coronary Syndrome and History of Aspirin Hypersensitivity

<table>
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<tbody>
<tr>
<td>We suggest a 2-step aspirin challenge for patients with a history of aspirin allergy to aid in the management of acute cardiovascular disease.</td>
<td>Conditional</td>
<td>Very Low</td>
</tr>
</tbody>
</table>

Conditional | Very Low
Rapid Aspirin Graded Challenge for Cardiovascular Emergencies

<table>
<thead>
<tr>
<th>Time</th>
<th>Dose</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 minutes</td>
<td>40.5mg</td>
<td>0 minutes</td>
</tr>
<tr>
<td>90 minutes</td>
<td>40.5mg*</td>
<td>90 minutes</td>
</tr>
</tbody>
</table>

* At this point, the goal of 81mg of aspirin has been reached. If the patient has no symptoms after a 90-minute period following the final dose, daily 81mg aspirin can be initiated. If at a later date higher doses of aspirin are indicated, administering 325mg with a 90 minute observation can be considered for non-AERD patients.

Some of Key Updates to Drug Allergy Parameter

- For antibiotics, de-emphasis on skin testing and increased role for drug challenge
- New recommendations on administration of beta-lactams in those with penicillin and cephalosporin allergies
  - Risk stratify based on anaphylactic history
- New recommendations for approach to co-trimoxazole allergy
- New recommendation for 2-step challenge rather desensitization for those with aspirin allergy with acute cardiovascular disease
Thank You

- Look for the Updated Drug Allergy Parameter Soon!
Eosinophilic Esophagitis Guidelines

David Stukus, MD, FACAAI
Director, Food Allergy Treatment Center
Professor of Clinical Pediatrics
Division of Allergy & Immunology
Nationwide Children’s Hospital
Columbus, Ohio

General Thoughts on Guidelines

An evidence based starting point
A guide and summary
May or may not apply to each patient
Individual Patients are NOT Research Participants

• WE are the clinicians
• WE have the understanding and expertise to apply our understanding of pathophysiology, diagnosis, and management to help GUIDE discussion of treatment options
• Our profession is filled with nuance, unanswered questions and a general inability to predict the future

• There are no guideline police!

Are These Patients the Same?

• 5 year old boy with recurrent abdominal pain despite daily PPI; biopsy shows 50 eos/hpf
• 38 year old woman seen in ED for solid food impaction but no chronic symptoms; biopsy shows 20 eos/hpf
• 25 year old man with intermittent abdominal pain and dysphagia; no prior treatment; biopsy shows 22 eos/hpf
• 11 year old girl with chronic constipation but no abdominal pain/emesis; biopsy shows 75 eos/hpf
Shared Decision Making


Focus on the Decision, Not the Outcome
EoE – International Guidelines

- AGREE conference – international consensus diagnostic criteria
  - Symptoms of esophageal dysfunction
    - Concomitant atopic conditions should increase suspicion for EoE
    - Endoscopic findings should increase suspicion for EoE
  - ≥15 eos/hpf (~60 eos/mm²) on esophageal biopsy
    - Eosinophilic infiltration should be isolated to the esophagus
  - Assessment of non-EoE disorders that cause or potentially contribute to esophageal eosinophilia
  - Acknowledges heterogeneity of phenotypes


EoE - Management

- Limitations in studies, esp. with lack of head to head comparisons
- Studies do not separate patients by phenotype

- Dietary elimination
- PPI therapy
- Corticosteroids
EoE - Prognosis

• Variable based upon age of presentation, heterogeneity of symptoms, endoscopy findings
• Long term monitoring is imperative for all patients
• Controversy: Treat towards symptomatic or histologic improvement?
• Who should stay on maintenance therapy?
  • Evidence of chronic remodeling
  • History of food impactions or severe symptoms
  • Rapid recurrence of symptoms if therapy is suspended

American Gastroenterological Association and the Joint Task Force on Allergy-Immunology Practice Parameters Clinical Guidelines for the Management of Eosinophilic Esophagitis

Hirano I1, Chan ES2, Rank M3, Sharaf R4, Stollman N5, Stukus D6, Wang K7, Greenhawt M,8 Falek-Ytter Y9

Acknowledgments

• **EoE Workgroup members (Technical and Guideline Writing Groups):** Ravi Sharaf, Glenn Furuta, Seema Aceves, Matthew Greenhawt, Jonathan Spergel, Yngve Falck-Ytter, Evan Dellon, Ikuo Hirano, Edmond Chan, Neil Stollman, Kenneth Wang, Matt Rank

• **JTF Members:** Jonathan Bernstein, Chitra Dinakar, David Golden, David Khan, Jay Lieberman, John Oppenheimer, Marcus Shaker, Dana Wallace, Julie Wang

Do You Know Your GRADE?

• Grading of Recommendations, Assessment, Development and Evaluations

• Transparent process

• Summary of evidence

• Systematic approach to make clinical practice recommendations

https://bestpractice.bmj.com/info/us/toolkit/learn-ebm/what-is-grade/recommendations
## What Can GRADE Do For You?

<table>
<thead>
<tr>
<th>What GRADE Does</th>
<th>What GRADE Does NOT Do</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decide what clinical question needs to be answered</td>
<td>Review all available evidence related to a condition or treatment</td>
</tr>
<tr>
<td>Determine outcomes that matter most</td>
<td>Identify all potential outcomes</td>
</tr>
<tr>
<td>Rate the quality of the evidence for each outcome</td>
<td>Provide yes/no answers</td>
</tr>
<tr>
<td>Provides actionable recommendations that vary in strength, according to the quality of evidence</td>
<td>Provide clear cut advice for every possible scenario</td>
</tr>
</tbody>
</table>

https://bestpractice.bmj.com/info/us/toolkit/learn-ebm/what-is-grade/

## For the Patient

<table>
<thead>
<tr>
<th>For the Patient</th>
<th>For the Clinician</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Strong</strong></td>
<td><strong>Most individuals should receive the recommended course of action</strong></td>
</tr>
<tr>
<td>Most individuals in this situation would want the recommended course of action and only a small proportion would not.</td>
<td>Formal decision aids are not likely to help individuals make decisions consistent with their values and preferences.</td>
</tr>
<tr>
<td><strong>Conditional</strong></td>
<td><strong>Different choices will be appropriate for different patients</strong>.</td>
</tr>
<tr>
<td>The majority of individuals in this situation would want the suggested course of action, but many would not.</td>
<td>Decision aids may be useful in helping individuals in making decisions consistent with their values and preferences. Clinicians should expect to spend more time with patients when working towards a decision.</td>
</tr>
<tr>
<td>Confidence Level</td>
<td>Description</td>
</tr>
<tr>
<td>------------------</td>
<td>-------------</td>
</tr>
<tr>
<td>High</td>
<td>We are <strong>very confident</strong> that the true effect lies close to that of the estimate of the effect.</td>
</tr>
<tr>
<td>Moderate</td>
<td>We are <strong>moderately confident</strong> in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.</td>
</tr>
<tr>
<td>Low</td>
<td>Our confidence in the effect estimate is <strong>limited</strong>. The true effect may be substantially different from the estimate of the effect.</td>
</tr>
<tr>
<td>Very Low</td>
<td>We have <strong>very little confidence</strong> in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Strength of Recommendation</th>
<th>Quality of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Recommendation:</strong> In patients with symptomatic esophageal eosinophilia, the AGA/JTF suggests using proton pump inhibition over no treatment</td>
<td>Conditional</td>
<td>Very low quality</td>
</tr>
<tr>
<td><strong>2. In patients with EoE, the AGA/JTF recommends topical glucocorticosteroids over no treatment</strong></td>
<td>Strong</td>
<td>Moderate</td>
</tr>
<tr>
<td><strong>3. In patients with EoE, the AGA/JTF suggests topical glucocorticosteroids rather than oral glucocorticosteroids</strong></td>
<td>Conditional</td>
<td>Moderate</td>
</tr>
</tbody>
</table>
4. In patients with EoE, the AGA/JTF suggests using elemental diet over no treatment

Comment: Patients who put a higher value on avoiding the challenges of adherence to an elemental diet and the prolonged process of dietary reintroduction may reasonably decline this treatment option.

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Strength of Recommendation</th>
<th>Quality of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>4. In patients with EoE, the AGA/JTF suggests using elemental diet over no treatment</td>
<td>Conditional</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

5. In patients with EoE, the AGA/JTF suggests using an empiric, six-food elimination diet over no treatment

Comment: Patients who put a higher value on avoiding the challenges of adherence to diet involving elimination of multiple common food staples and the prolonged process of dietary reintroduction may reasonably decline this treatment option.

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Strength of Recommendation</th>
<th>Quality of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>5. In patients with EoE, the AGA/JTF suggests using an empiric, six-food elimination diet over no treatment</td>
<td>Conditional</td>
<td>Low</td>
</tr>
</tbody>
</table>
6. **Recommendation**: In patients with EoE, the AGA/JTF suggests using an allergy testing-based elimination diet over no treatment

**Comment**: Due to the potential limited accuracy of currently available, allergy-based testing for the identification of specific food triggers for EoE, patients may prefer alternative medical or dietary therapies to an exclusively testing-based elimination diet.

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Strength of Recommendation</th>
<th>Quality of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>6. In patients with EoE, the AGA/JTF suggests using an allergy testing-based elimination diet over no treatment</td>
<td>Conditional</td>
<td>Very low quality</td>
</tr>
</tbody>
</table>

7. **Recommendation**: In patient with EoE in remission following short-term use of topical glucocorticosteroids, the AGA/JTF suggests continuation of topical glucocorticosteroids over discontinuation of treatment

**Comments**: Patients who put a high value on the avoidance of long-term topical steroid use and its possible associated adverse effects, and/or place a lower value on the prevention of potential long-term undesirable outcomes (i.e. recurrent dysphagia, food impaction, and esophageal stricture), could reasonably prefer cessation of treatment after initial remission is achieved, provided clinical follow-up is maintained.

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Strength of Recommendation</th>
<th>Quality of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>7. Recommendation: In patient with EoE in remission following short-term use of topical glucocorticosteroids, the AGA/JTF suggests continuation of topical glucocorticosteroids over discontinuation of treatment</td>
<td>Conditional</td>
<td>Very low quality</td>
</tr>
<tr>
<td>Recommendation</td>
<td>Strength of Recommendation</td>
<td>Quality of Evidence</td>
</tr>
<tr>
<td>--------------------------------------------------------------------------------</td>
<td>------------------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>8. Recommendation: In adult patients with dysphagia from a stricture associated with EoE, the AGA/JTF suggests endoscopic dilation over no dilation</td>
<td>Conditional</td>
<td>Very low quality</td>
</tr>
<tr>
<td>9. Recommendation: In patients with EoE, the AGA/JTF recommends using anti-IL-5 therapy for EoE only in the context of a clinical trial</td>
<td>No recommendation</td>
<td>Knowledge gap</td>
</tr>
<tr>
<td>10. Recommendation: In patients with EoE, the AGA/JTF recommends using anti-IL-13 or anti-IL-4 receptor alpha therapy for EoE only in the context of a clinical trial</td>
<td>No recommendation</td>
<td>Knowledge gap</td>
</tr>
<tr>
<td>11. Recommendation: In patients with EoE, the AGA/JTF suggests against the use of anti-IgE therapy for EoE</td>
<td>Conditional</td>
<td>Very low quality</td>
</tr>
<tr>
<td>12-15. Recommendation: In patients with EoE the AGA/JTF suggest using montelukast, cromolyn sodium, immunomodulators, and anti-TNF for EoE only in the context of a clinical trial</td>
<td>No recommendation</td>
<td>Knowledge gap</td>
</tr>
</tbody>
</table>
The Role of the Allergist

- Clarify diagnosis and other causes of eosinophilia
- Discuss potential role of food allergens and options for identifying foods to avoid
- Discuss risk/benefit of various treatment choices
- Review prognosis, need for follow up and long term monitoring

- Help guide shared decision making
- Expect to spend more time with patients while working towards a decision

Synthesis Approach: For the Allergist

- PPI
- Steroid
- Diet
- SDM/DA/Conversation
- Specific choices
  - Drug, strength, dietary options
- Reassess
  - Try other options
Unanswered Questions

- How do EoE management choices compare with each other head-to-head?
- What are long term data regarding efficacy & safety?
- Can we identify an optimal candidate for each treatment option according to predicted response to therapy AND adherence?
- Can we design and implement effective decision aids for management of EoE?

Final Thoughts…

Implications for Practice

- Review & reference EoE guidelines to better understand the evidence surrounding management choices
- Develop and practice a shared decision making approach to help guide patients with EoE
- Evidence regarding one clear management option is lacking

Summary

- Eosinophilic esophagitis is a heterogeneous condition with varied treatment approaches
- Allergists can play an important role in helping patients understand the nuances involved in management and monitoring
- Guidelines are guidelines, not a specific map for every patient
Thank You
NHLBI 2020 Focused Updates to the Asthma Management Guidelines

Alan P. Baptist, MD, MPH
Associate Professor of Medicine
Director, UM Comprehensive Asthma Management Program

Learning objectives

- To understand the process in developing the new Asthma Management Guidelines
- To learn how to apply changes in asthma diagnosis, monitoring, and treatment based on evidence and shared decision making
- To determine both the strengths and limitations of the new Asthma Management Guidelines
Timeline for Asthma Guidelines 2020 Update

Members of the NAEPP Expert Panel

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University of Michigan

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University of Chicago
Focused Updates, Not Complete Revision of 2007 Guidelines

- Improve asthma management and support informed, shared decision making
- New guidance in six key areas of asthma diagnosis, management, and treatment
- Updates offer 19 recommendations

GRADE Methodology

Grading of Recommendations Assessment, Development and Evaluation (GRADE):

- Framework to determine quality or certainty of evidence and direction and strength of a recommendation.
- Used patient-centered outcomes to make judgments:
  - Critical outcomes: exacerbations, asthma control, asthma-related quality of life
  - Important outcomes: asthma symptoms, rescue med use, others by topic
GRADE Methodology

- 2 main components to GRADE:
  - Creation of Evidence Profiles based upon each critical and important outcome.
  - Development of an Evidence to Decision Table for each recommendation.

Direction and Strength of Recommendation

Evidence-to-Decision (EtD) tables determined direction of each recommendation (for or against intervention) and its strength (strong or conditional).

<table>
<thead>
<tr>
<th>Implications</th>
<th>Strong Recommendation</th>
<th>Conditional Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>For patients</td>
<td>Most would want; only small proportion would not.</td>
<td>Most would want, but many would not.</td>
</tr>
<tr>
<td>For clinicians</td>
<td>Most patients should receive intervention. Formal decision aids likely unnecessary.</td>
<td>Different choices appropriate based on individual values and preferences. Decision aids may be helpful.</td>
</tr>
<tr>
<td>For policy makers</td>
<td>Recommendation can be adapted as policy or performance measure.</td>
<td>Will require substantial debate and involvement of stakeholders.</td>
</tr>
<tr>
<td>For researchers</td>
<td>Supported by credible research. For low/very low certainty of evidence, new research may provide evidence to alter recommendation.</td>
<td>Likely to be strengthened by additional research.</td>
</tr>
</tbody>
</table>
Topic Areas

1. Intermittent Inhaled Corticosteroids
2. Long-Acting Muscarinic Antagonists
3. Indoor Allergen Mitigation
4. Immunotherapy in the Treatment of Allergic Asthma
5. Fractional Exhaled Nitric Oxide Testing
6. Bronchial Thermoplasty

Intermittent ICS – Question 1

- You see a 3 year old child who presents with occasional wheezing. Should you use intermittent ICS during these episodes?
Intermittent ICS – Question 1

• For children ages 0–4 years with **recurrent wheezing triggered by respiratory tract infections only and no wheezing between infections**, the Expert Panel conditionally recommends
  – a **short course of daily ICS** at the onset of a respiratory tract infection
  – with an inhaled **short-acting beta$_2$-agonist** (SABA) as-needed

(Conditional recommendation, high certainty evidence)

Intermittent ICS – Question 2

• Part 2a
  – In patients with persistent asthma, does increasing the ICS dose during an asthma worsening help?
    • Yes
    • No
Intermittent ICS – Question 2a

- For children ages 4 years and older and adults with mild to moderate persistent asthma who are likely to be adherent to daily ICS treatment, the Expert Panel conditionally recommends against a short-term increase in the ICS dose for increased symptoms or decreased peak flow. (Conditional recommendation, low certainty evidence.)

Intermittent ICS – Question 2b

- Mild persistent asthma management guidelines
- A 25-year-old with asthma is using albuterol 3-4X/week, wakes up 1X/week, and FEV is 83%. What would you do?
  a) Medium dose ICS/formoterol daily and as needed
  b) LTRA daily
  c) Albuterol and ICS as needed
  d) Daily medium dose ICS
Intermittent ICS – Question 2b, mild asthma

• For individuals > age 12 with mild persistent asthma, either of the following two treatments are recommended:
  – a daily low-dose ICS and as-needed SABA for quick-relief therapy, or
  – intermittent as-needed ICS and SABA used one after the other for worsening asthma.

(Conditional recommendation, moderate certainty evidence.)

Intermittent ICS – Q3

• Now the moderate and severe persistent asthma patients – can I use an ICS/LABA as their only inhaler?
Intermittent ICS – Q2b, mod/severe asthma

- For individuals ages 4 years or older with moderate to severe persistent asthma, preferred treatment is a single inhaler with ICS-formoterol used both daily and as-needed. (Strong recommendation, high certainty evidence for ages ≥ 12 years, moderate certainty evidence for ages 4–11 years.)

- For individuals ages 12 years or older with moderate to severe persistent asthma, preferred treatment is a single inhaler with ICS-formoterol used both daily and as-needed compared to daily higher dose ICS-long-acting bronchodilator combination with as-needed SABA. (Conditional recommendation, high certainty evidence.)

- BOTTOM LINE – Use ICS/formoterol as controller and reliever for your moderate to severe persistent asthma patients

LAMA therapy in those age > 12

- 3 questions:
  - Patient on ICS alone, is LAMA as good as adding LABA?
  - Patient on ICS alone, what is a good step up option?
  - Patient on ICS + LABA, will LAMA help?
LAMA therapy in those age > 12

- If asthma not controlled by ICS therapy alone, **adding a LABA rather than a LAMA** to an ICS is recommended. (Conditional recommendation, moderate certainty.)

    ![Diagram](ICS + LABA > ICS + LAMA)

- If a LABA cannot be used (unable to tolerate, contraindication, inability to use device, unavailability) **adding a LAMA to an ICS is an acceptable alternative.** (Conditional recommendation, moderate certainty.)

    ![Diagram](ICS + LAMA > ICS + nothing)
LAMA therapy question

• A patient is on an ICS-LABA combination but not fully controlled. Adding a LAMA is recommended, as it has shown benefit
  A. True
  B. False

LAMA therapy in those age > 12

• If asthma is not controlled with ICS-LABA, adding a LAMA is recommended for many people because it offers a small potential benefit. (Conditional recommendation, moderate certainty.)

\[
\text{ICS + LABA + LAMA} \succ \text{ICS + LABA}
\]
Indoor Allergen Mitigation

• Does control of the indoor environment help in asthma? What is best way to do so? Should we do for everyone?

Indoor Allergen Mitigation

• For individuals with asthma with no history of exposure and no allergies (IgE or sensitization) or symptoms after exposure to indoor allergens, environmental interventions in the home are not recommended. (Conditional recommendation, low certainty evidence.)

• For individuals with asthma who are exposed and allergic to a specific indoor substance using multiple strategies to reduce the allergen is recommended—using only one strategy often does not improve asthma outcomes. (Conditional recommendation, low certainty evidence.)

• For individuals with asthma who are sensitive to dust mites, impermeable pillow/mattress covers are recommended only as part of a multicomponent intervention. (Conditional recommendation, moderate certainty of evidence.)

• Integrated pest management in the home is recommended for individuals with asthma who are allergic and exposed to cockroaches, mice, or rats. (Conditional recommendation, low certainty evidence.)
Indoor Allergen Mitigation

<table>
<thead>
<tr>
<th>Intervention assessed in studies in the SR</th>
<th>Animal dander</th>
<th>Dust mites</th>
<th>Cockroaches</th>
<th>Mold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acanthicide</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Air filtration systems and air purifiers</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Carpet removal</td>
<td>++</td>
<td>++</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Cleaning products (e.g., bleach)</td>
<td>++</td>
<td>+</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>HEPA vacuum cleaners</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Impermeable pillow and mattress covers</td>
<td>++</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Integrated pest management</td>
<td>*</td>
<td>++</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mold mitigation</td>
<td></td>
<td></td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>Pet removal</td>
<td>++</td>
<td></td>
<td></td>
<td>+</td>
</tr>
</tbody>
</table>

Immunotherapy for asthma

- Should I use subcutaneous immunotherapy (SCIT) for asthma? What about sublingual immunotherapy (SLIT)?
Immunotherapy for asthma

- Subcutaneous immunotherapy is recommended as an adjunct treatment to standard pharmacotherapy for individuals with mild-moderate allergic asthma who have demonstrated allergic sensitization and evidence of worsening asthma symptoms after exposure to relevant antigen(s). (Conditional recommendation, moderate certainty evidence.)

Immunotherapy for asthma

- In patients with mild asthma, the evidence supports SLIT with house dust mite
  a) True
  b) False
Immunotherapy for asthma

- Evidence reviewed did not support using sublingual immunotherapy to specifically treat allergic asthma. (Conditional recommendation, moderate certainty evidence.)

FENO Testing in Asthma

- Can FENO help to diagnose asthma? Will it predict wheezing toddlers who will develop asthma? Should it be routinely used in choosing medications or monitoring response?
FENO Testing in Asthma

• You have a patient and are unclear if asthma is present after spirometry, history, and physical exam. FENO can help make the diagnosis.
  a) True
  b) False

FENO Testing in Asthma

• FeNO measurement may support a diagnosis of asthma in those age ≥ 5 for whom the diagnosis is uncertain even after a complete history, physical examination, and spirometry testing including bronchodilator responsiveness. (Conditional recommendation, moderate certainty evidence.)

• May be used as part of ongoing asthma monitoring and management when there is uncertainty in adjusting therapy using clinical and laboratory assessment. (Conditional recommendation, low certainty evidence.)

• Should not be used in isolation to assess asthma control, predict a future asthma exacerbation, or assess the severity of an exacerbation. (Strong recommendation, low certainty evidence.)
FENO Testing in Asthma

Table II: Interpretations of FeNO Test Results for Asthma Diagnosis in Nonsmoking Individuals Not Taking Corticosteroids*

<table>
<thead>
<tr>
<th>FeNO Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;25 ppb</td>
</tr>
<tr>
<td>(&gt;20 in children ages 5-12)</td>
</tr>
<tr>
<td>25-50 ppb</td>
</tr>
<tr>
<td>(20-35 in children ages 5-12)</td>
</tr>
<tr>
<td>&gt;50 ppb</td>
</tr>
<tr>
<td>(&gt;35 in children ages 5-12)</td>
</tr>
</tbody>
</table>

FENO Testing in Asthma

- In children ages 4 years and younger who have recurrent episodes of wheezing, FeNO measurement does not predict the future development of asthma. (Strong recommendation, low certainty evidence.)
Bronchial Thermoplasty

• In adult patients with uncontrolled asthma, should I perform bronchial thermoplasty?

35

Bronchial Thermoplasty

• Most individuals 18 years and older with uncontrolled asthma should not undergo bronchial thermoplasty because benefits are small, risks are moderate, and long-term outcomes are uncertain. (Conditional recommendation, low certainty evidence.)

• Some individuals with persistent asthma may be willing to accept the risks of bronchial thermoplasty and, therefore, might choose this intervention after shared decision making with their health care provider.
### Stepwise table ages 0-4

**Figure 1b:** Stepwise Approach for Management of Asthma in Individuals Ages 0-4 Years

<table>
<thead>
<tr>
<th>Treatment</th>
<th>STEP 1</th>
<th>STEP 2</th>
<th>STEP 3</th>
<th>STEP 4</th>
<th>STEP 5</th>
<th>STEP 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preferred</td>
<td>PRN SABA</td>
<td>Daily low-dose ICS and PRN SABA</td>
<td>Daily low-dose ICS and PRN SABA</td>
<td>Daily medium-dose ICS LABA and PRN SABA</td>
<td>Daily high-dose ICS LABA and PRN SABA</td>
<td></td>
</tr>
<tr>
<td></td>
<td>and at the start of RTI: Add short course daily ICS</td>
<td>and PRN SABA</td>
<td>or Daily low-dose ICS and PRN SABA</td>
<td>or Daily medium-dose ICS and PRN SABA</td>
<td>or Daily high-dose ICS and PRN SABA</td>
<td></td>
</tr>
<tr>
<td>Alternative</td>
<td>Daily montelukast* or Cromolyn* and PRN SABA</td>
<td>Daily medium-dose ICS LABA and PRN SABA</td>
<td>Daily high-dose ICS LABA and PRN SABA</td>
<td>Daily high-dose ICS LABA and PRN SABA</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Assess Control
- First check adherence, inhaler technique, environmental factors, and comorbid conditions.
- Step up if needed, reassess in 4-6 weeks.
- Step down if possible (if asthma is well controlled for at least 3 consecutive months).

Consult with asthma specialist if Step 3 or higher is required. Consider consultation at Step 2.

Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual’s clinical situation.

### Stepwise table ages 5 - 11

**Figure 1c:** Stepwise Approach for Management of Asthma in Individuals Ages 5-11 Years

<table>
<thead>
<tr>
<th>Treatment</th>
<th>STEP 1</th>
<th>STEP 2</th>
<th>STEP 3</th>
<th>STEP 4</th>
<th>STEP 5</th>
<th>STEP 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preferred</td>
<td>PRN SABA</td>
<td>Daily low-dose ICS and PRN SABA</td>
<td>Daily low-dose ICS and PRN SABA</td>
<td>Daily medium-dose ICS LABA and PRN SABA</td>
<td>Daily high-dose ICS LABA and PRN SABA</td>
<td></td>
</tr>
<tr>
<td></td>
<td>and at the start of RTI: Add short course daily ICS</td>
<td>and PRN SABA</td>
<td>or Daily low-dose ICS and PRN SABA</td>
<td>or Daily medium-dose ICS and PRN SABA</td>
<td>or Daily high-dose ICS and PRN SABA</td>
<td></td>
</tr>
<tr>
<td>Alternative</td>
<td>Daily LTRA* or Cromolyn* or Ipratropium* and PRN SABA</td>
<td>Daily medium-dose ICS LABA or Daily low-dose ICS and PRN SABA</td>
<td>Daily high-dose ICS LABA or Daily low-dose ICS and PRN SABA</td>
<td>Daily high-dose ICS LABA or Daily low-dose ICS and PRN SABA</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Assess Control
- First check adherence, inhaler technique, environmental factors, and comorbid conditions.
- Step up if needed, reassess in 4-6 weeks.
- Step down if possible (if asthma is well controlled for at least 3 consecutive months).

Consult with asthma specialist if Step 3 or higher is required. Consider consultation at Step 2.

Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual’s clinical situation.
Stepwise table ages > 12

Guideline Provider resources
Patient and caregiver resources

nhlbi.nih.gov/BreatheBetter

Questions?