Allergy Symposium
Saturday, November 14, 2015
Aspirin Exacerbated Respiratory Disease: Indications, Protocols, Pitfalls
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Disclosures

• No relevant financial disclosures or conflicts of interest related to this talk
• Off label use of medication: aspirin for the treatment of aspirin exacerbated respiratory disease (AERD), experimental Xolair for AERD, zileuton and montelukast for AERD desensitizations
Objectives

• Review pathophysiology of AERD
• Review indications for aspirin desensitization in AERD
• Review commonly used protocols for aspirin desensitization/challenge
• Identify areas of difficulty in conducting aspirin desensitizations
Aspirin Exacerbated Respiratory Disease (AERD)

- Also known as Samter’s triad and Triad Asthma
- Asthma, Chronic sinusitis with nasal polyps (CRSwNP), and Aspirin Sensitivity
- 15-40% of patients with asthma and CRSwNP
  - < 5-9% of asthmatics
  - 15% of CRSwNP
- Aspirin or COX1 ingestion produces characteristic symptoms
- COX2 inhibitors usually tolerated

AERD Clinical Symptoms

- Historically after a severe cold
- Usually present in 3\textsuperscript{rd}-4\textsuperscript{th} decade of life
- Often CRSwNP then asthma
  - Asthma often severe persistent
  - CRSwNP difficult to treat despite intensive topical and systemic steroids, local treatment, and surgery
- ASA/NSAID sensitivity presents at any point

AERD Clinical Symptoms

TABLE E1. Features strongly associated with AERD

- Severe persistent asthma
- Complete anosmia
- Pansinusitis on imaging
- Nasal polyposis refractory to sinus surgery (multiple surgeries)
- Age of onset in fourth decade
- Incomplete response to antibiotics or corticosteroids
- Respiratory reaction to any NSAID or aspirin

Formal diagnosis requires supervised ASA challenge
- 15% of those with AERD unaware of ASA/NSAID sensitivity until clinical challenge

Symptoms upon ASA/NSAID ingestion

- Naso-ocular: rhinorrhea, congestion, sneezing, ocular tearing, conjunctival injection, angioedema, laryngospasm
- Lower respiratory: bronchospasm
  - Can be very severe requiring intubation
- Less frequent
  - Abdominal pain and cramping
  - Hypotension
  - Hives

AERD Clinical Symptoms

- Alcohol induced symptoms
  - Higher likelihood of upper and lower respiratory symptoms with AERD than ASA-tolerant asthma, ASA-tolerant CRS, normal controls

- Symptom-based clustering with SNOT-22 in AERD
  - Severe overall, severe sino-nasal scores (mean 90.8, 62)
  - Severe overall score associated with rapid relapse symptoms post-surgery

- Tolerance of ASA 81 mg does not rule out AERD

Cardet, 2015; Divekar, 2015; Lee-Sarwar, 2015
Treatment of AERD

- Topical nasal steroid preparations
- Inhaled steroid/LABA
- SABA
- Leukotriene antagonist/modifier
- Systemic corticosteroid
- Surgical interventions
- Aspirin desensitization
# Specific NSAIDS and AERD

<table>
<thead>
<tr>
<th>Cross-reacting NSAIDs in AERD, COX-1 inhibitors</th>
<th>Drugs that do not cross-react with ASA in patients with AERD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>Sodium salicylate</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>Salicylamide</td>
</tr>
<tr>
<td>Nabumetone</td>
<td>Choline magnesium</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>Azapropazone</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>Dextropropoxyphene</td>
</tr>
<tr>
<td>Naproxen</td>
<td>Celecoxib</td>
</tr>
<tr>
<td>Difunisal</td>
<td>Parecoxib</td>
</tr>
<tr>
<td>Ketoprofen</td>
<td>Lumaricoxb</td>
</tr>
<tr>
<td>Piroxicam</td>
<td>Acetaminophen*</td>
</tr>
<tr>
<td>Etodolac</td>
<td>Meloxicam*</td>
</tr>
<tr>
<td>Ketorolac</td>
<td>Highly selective COX-2 inhibitors and non-COX inhibitors are generally well tolerated in patients with AERD.</td>
</tr>
<tr>
<td>Sulindac</td>
<td>*At higher doses (&gt;1000 mg of acetaminophen or 15 mg of meloxicam) these NSAIDs can inhibit COX-1 but are generally well tolerated.</td>
</tr>
<tr>
<td>Fenoprofen</td>
<td></td>
</tr>
<tr>
<td>Meclofenamate</td>
<td></td>
</tr>
<tr>
<td>Tometin</td>
<td></td>
</tr>
<tr>
<td>Flurbiprofen</td>
<td></td>
</tr>
<tr>
<td>Mefenamic acid</td>
<td></td>
</tr>
</tbody>
</table>
Burden of AERD

- Worse pre-operative sinus CT and endoscopy scores than other CRS, higher post-operative symptom score, 10x higher rate of repeat sinus surgery
  - Average 3 sinus surgeries per AERD patient
- Asthma: lower mean post-bronchodilator FEV1, more severe asthma, high rates of high-dose ICS, higher intubation rates
  - 8% of intubations for asthma due to NSAID
  - Higher rates of daily prednisone use
- Possible avoidance of beneficial ASA/NSAIDs for cardiac disease and pain relief
  - Substitution for more expensive agents

Kaiser Permanente
Chang (1), 2012.
Burden of AERD

• Quality of life: survey based patient reported largest impacts
  – Sinonasal symptoms
  – Sense of smell
    • Enjoyment of food/eating

• 70% reported moderate negative quality of life

• Daily ASA therapy felt to most effective treatment

• Why patients stopped? 43% due to stopping for surgery

Ta, 2015; Laidlaw, 2015
Mechanism of AERD

• Overproduction of CysLT due to increased expression of LTC4 synthetase
  – Baseline increased production of CysLT
    • Especially increased urinary LTE4
    – Increased PGD2 $\rightarrow$ bronchoconstriction
    – Acute increase in CysLT with ingestion of ASA/NSAIDs

• Increased numbers of CysLT type 1 receptors on tissue

Steinke, 2009; White, 2012; Steinke, 2013; Woesnner, 2014.
Mechanism of AERD

• Higher levels of IFN-gamma from eosinophils
  – Promotes maturation of eosinophils, increase gene expression for leukotriene synthesis

• NSAIDS cause decreased PGE2 production due to COX-1 inhibition
  – increased 5-lipoxygenase and FLAP activity → Increased leukotriene synthesis
    • LTB4/C4/D4/E4
  – Decreased mast cell stability → increased histamine and tryptase release

• Cells involved: eosinophils, mast cells, platelets

Mechanism of AERD

FIG E1. Schematic of the arachidonic acid pathway and associated findings in AERD pathophysiology, with increased levels of cysteinyl leukotrienes and their receptors, underproduction of prostaglandin E2 (PGE2), and effect of aspirin/NSAID inhibition of COX-1 shown. FLAP, 5-lipoxygenase-activating protein; 5-LO, 5-lipoxygenase; LT, leukotriene; TX, thromboxane.
Who should undergo ASA desensitization?

- Patients with AERD with moderate-severe asthma and/or intractable nasal congestion despite topical corticosteroid, LTMD, ICS/LABA
- AERD with severe nasal polyp disease
- Patients needing continuous or frequent systemic corticosteroid to control AERD
- Patients with AERD who need aspirin/NSAID for other disease processes (i.e. CAD, inflammatory disease)

Stevenson, 2006.
Evidence for Aspirin Desensitization

• EPOS 2012: grade D recommendation due to lack of high-grade evidence
• High-grade evidence is limited due to difficulty in performing RCT
  – Patients experience provoking dose during desensitization and purportedly noticeable effect of return of nasal congestion upon discontinuation of ASA for placebo
• Small double blind crossover trial
  – 3 months with 1 month wash out: less nasal symptoms and less nasal steroid use
  – No change in respiratory parameters

Fokkens, 2012; Stevenson, 1996; Stevenson, 1984.
Clinical effects of ASA desensitization

- Reduction in number of sinus infections/year
- Reduction in hospitalizations for asthma/yr
- Improvement in smell
- Reduction in use of systemic corticosteroids
- Number of sinus and polyp operations/yr (avg of 1 surgery in 3yrs → 1 in 10 years)

Stevenson, 1996.
Short-term effects of ASA desensitization

- Improvement in nasal and asthma scores and smell in 4 weeks
- By the first 6 months of ASA treatment
  - reduction in sinus infections
  - short courses of prednisone
  - improved smell and results persisted
  - Mean prednisone dose 10.8mg/d → 8.1 mg/day at 6 months → 3.6 mg/d after 1 year

Mechanism of ASA desensitization

- ASA desensitization leads to decreased leukotriene synthesis and down regulation of CysLT1R
  - How? ASA inhibits T cell IL4 expression
    - IL4 → IL4 receptor → Induces activation of STAT6 via Janus kinases
    - STAT6 site on CysLT1R promoter and maybe on the LTC4 synthetase gene
- ASA may also inhibit activation of STAT6 by modulating NF-KB in activated T cells
- During ASA desensitization
  - Elevation of ENO and sputum tryptase
  - 6 months after: decrease in sputum IL-4 and MMP-9 and increase in FLT3-L

Contraindications to ASA desensitization

- Pregnancy
- Unstable asthma
- Gastric ulcer
- Bleeding disorders
- Possible concomitant anti-coagulant agents
  - Warfarin
- Relative: patient compliance, multiple comorbidities
Preparation for ASA desensitization

- Recent spirometry
  - FEV1 > 70% of patient’s personal best
  - FEV1 > 1.5L absolute

- Practice paper recommends, FEV1 q 1 hour for 3 hours to establish <10% variability

- Start ICS/LABA if asthma poorly controlled

- Start LTMDs

- Discontinue anti-histamines 48 hours prior
  - Also SABAs prior and inhaled anti-cholinergic

- Consider adding/increasing oral steroid

- Obtain informed consent

LTMDs

- Montelukast, zafirlukast = leukotriene (CysLT1) receptor antagonist
- Zileuton (5-lipoxygenase inhibitor)
- LTMDs seem to block lower respiratory tract reactions but not upper in challenges to ASA, effect may be more robust when combined with ICS/LABA as well
  - Therefore can challenge patient’s on LTMDs without fear of false negatives and makes desensitization safer/quicker
  - 201 montelukast, 40 zafirlukast, 14 zileuton, 5 combo zileuton + LTRA
- Fewer patients taking LTMDs had a more than 20% decline in FEV1 compared with those not taking
  - Effect of LTMD present regardless of systemic corticosteroids
  - 201 montelukast, 39 zafirlukast, 14 zileuton, 6 combination vs 417 not taking LTMD

LTMDs

• LTMD non-use associated with moderate-large bronchial reactions during oral ASA challenges
  – 25/278 on LTMD had mod-severe bronchial reactions (>21% decrease in FEV1) OR 0.57 vs 37/147 not on LTMD OR 1.75
  – Did not specify which ones used, only that “most commonly LT receptor antagonist used”

• Limited number of patients on 5-lipoxygenase inhibitors
  – 6 patients on zileuton 600 mg 4x/day for 7 days prior to ASA challenge ➔ All six reacted, no statistical change in provocation dose, 4/6 had bronchospasm, urine LTE4 increased

Traditional Oral Protocol

- Limitations of oral protocol:
  - Usual time to reaction after provoking dose 102 minutes
  - Must repeat provoking dose
  - Need 3 hour time intervals

<table>
<thead>
<tr>
<th>Time</th>
<th>Day 1 mg</th>
<th>Day 2 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 AM</td>
<td>20-40 mg*</td>
<td>100-160 mg</td>
</tr>
<tr>
<td>11 AM</td>
<td>40-60 mg</td>
<td>160-325 mg</td>
</tr>
<tr>
<td>2 PM</td>
<td>60-100 mg</td>
<td>325 mg</td>
</tr>
</tbody>
</table>

- Confirm that the patient's baseline FEV₁ is the same as the prior best value and that they have not used their albuterol rescue inhaler in the past week. If not, consider 1-day placebo challenge to determine stability of airways.
- *Choice of dosing: lower dose is chosen if the patient is not using a leukotriene-modifying drug, has a low baseline FEV₁, and has had a recent hospitalization or emergency department visit for asthma.
- By using a pill cutter, an 81-mg ASA tablet can be cut into a half or a fourth.
- Measure FEV₁ every hour and wait 3 hours between doses.
- FEV₁ should be at ≥1.5 L and >60% of predicted value.
- After a reaction has been treated and resolved, go to step “a.”
  a. Repeat the ASA provoking dose.
  b. If no reaction, continue to escalate dose every 3 hours as above.
  c. At 325 mg of ASA, desensitization/tolerance is complete.
  d. Patient should be instructed to start 650 mg of ASA that night as their first dose and continue with 650 mg twice daily.

This is one of many published protocols for aspirin desensitization. Lower starting doses of aspirin are provided for patients who are not pretreated with a leukotriene-modifying drug or have a low FEV₁. Otherwise, a higher starting dose can be chosen.
Positive challenge

- Naso-ocular symptoms
- Laryngospasm
- 15% decline or greater in FEV1
- Cutaneous-hives/flushing
- GI symptoms – abdominal pain, nausea
- Systemic reaction- hypotension
- Negative reaction
  - No reaction after 325 mg of ASA
- Treat with:
  - Anti-histamines, albuterol, H2-blockers, intra-nasal anti-histamines/topical decongestants, nebulized racemic epinephrine, epinephrine IM

ASA therapy in AERD

- **AERD treatment**
  - Usual post-desensitization dose ASA 650mg BID
  - Some patients can decrease to 325 BID
  - Some can go further down but benefits may decrease

- **Cardio-protection**
  - 81 mg daily

- **Remain desensitized to other COX-1 inhibitors**
  - ASA 325 mg daily

- **If lapse in therapy**
  - >96 hours- repeat desensitization
  - 72-96 hours- 325 mg in monitored setting
  - 48-72 hours refractory period

AERD treatment algorithm

1. Suspect AERD
   - Consider diagnostic aspirin or ketorolac challenge
   - Is patient a candidate for aspirin therapy?
     - No
     - Low suspicion for AERD
       - Patient does not have AERD
         - Treat empirically with aspirin and monitor closely for response
       - High suspicion for AERD
         - Consider second challenge without montelukast pretreatment
     - Yes
       - Nonreactor
         - No reason to suspect abdominal upset from aspirin
         - Discharge patient on 65mg twice daily
         - Reduce gradually to 325mg twice daily. Increase to previously effective dose if necessary
       - Reactor
         - History of gastritis or dyspepsia with NSAIDs
         - Consider starting PPI therapy
         - Discharge at 325mg of aspirin daily and consider increasing the dose at monthly follow-up
   - Evaluate extent of sinus disease and if polypectomy necessary consider surgery before desensitization
   - Ensure the patient is optimized prior to desensitization (FEV1 >70%, asthma optimally controlled with systemic steroids if necessary, and montelukast/zafrilukast prophylaxis)
   - Perform aspirin challenge/desensitization
Side effects of ASA therapy

• Bleeding complications
• ASA induced urticaria
• Gastric issues
  – GI bleeding
  – Ulcer
  – Gastritis/abdominal pain
  – Pancreatitis- few cases reported (controversial)
• Compliance with therapy
  – Risk of severe reaction if missed multiple days of therapy

Berges-Gimeno, 2003; Durrani, 2013; Hoyte, 2012; Stevenson, 2012
KP AERD aspirin desensitization

• Currently being conducted inpatient in the ICU/CCU at LAMC
• Will be implementing outpatient oral protocol
  – Low risk patients
• Requirements to conduct safely:
  – Supervising allergist comfortable conducting and treating aspirin reactions
  – Adequate nursing and pharmacy support
  – Dedicated clinic space to conduct
Outpatient vs inpatient

• Inpatient
  – Severe asthma
  – Recent MI
  – Other complicating medical diagnosis or situation

• History of life-threatening reaction
  – Per 2007 practice paper, should be inpatient
  – Per Scripps, history of severe asthmatic reaction did not predict severe reaction during oral challenge and only 13% of OAC had ≥30% decline in FEV1

• Outpatient
  – Dedicated staff versed in treating severe asthma attacks
  – Continuous cardiopulmonary monitoring, spirometry
  – Capability for CPR, ventilator management
  – IV access
    • Per Scripps, never had to use IV (unpublished data)

Chang, 2012; Williams, 2007; Macy, 2007
Barriers to Conducting Desensitizations

- Time and resources needed to conduct desensitization
  - 1:1 nursing
  - Can turn into 3 days
  - Consideration for overnight accommodation

- Cost for patients - travel expenses, lost work time
  - Inpatient: hospital admission
  - Outpatient: might be less
Potential pitfalls of therapy

• Failed desensitization
  – Conversion to inpatient, systemic steroids, zileuton
  – Non-compliance with LTMDs

• Silent desensitization
  – LTMDs, particularly montelukast

• Failed response
  – Patient expectations
  – Conducting ASA therapy prior to reducing polyp burden

• Routine procedures
  – Need to stop aspirin
Alternate protocols

• Might be safer
• Likely faster
Intranasal ketorolac?

• In Europe, intranasal aspirin-lysine used for establishment of aspirin sensitivity via challenge
  – Not available in the United States
• Ketorolac- NSAID with COX1 and 2 inhibition capability
  – Approved for intramuscular, IV, oral, ophthalmic use
  – Most recently approved for intra-nasal use for pain management
    • Sprix (ketorolac tromethamine) 15.75 mg/spray
Intranasal ketorolac for diagnosis

- 29 patients with suspected AERD challenged with nasal ketorolac before oral challenge and desensitization
- Dose of 2.1, 5.2, 7.8 mg ketorolac given → usual oral challenge
- 18/29 patients with positive oral challenge
  - 14/18 had positive ketorolac challenge
  - 4/18 had negative ketorolac
- 4/29 patient positive ketorolac but negative oral
  - Suggesting that desensitization has already occurred
- 7/29 negative oral and intranasal challenge
- → ketorolac had sensitivity 78%, specificity 64%

White, 2006.
“Use of intranasal ketorolac and modified oral aspirin challenge for desensitization of aspirin-exacerbated respiratory disease”

• 100 consecutive patients from 2007-2009 with history of AERD referred to Scripps for ASA challenge/desensitization
  – Provocative response defined as conjunctivitis, rhinitis, laryngospasm, bronchospasm, ≥20% decrease in nasal flow rate, ≥15% drop in FEV1
    • only these included in results

• Compared outcomes between these patients versus historical controls similar 100 controls 2003-2004 undergoing standard oral
How to make intranasal ketorolac?

Table 1. Steps to Prepare Ketorolac Nasal Spray

1. Take ketorolac tromethamine (60 mg/2 mL) and preservative-free normal saline (2.75 mL).
2. Mix in an emptied spray bottle.
3. Prime with 5 sprays before use, then each spray actuates 1.26 mg of solution.
4. Instruct patient and medical personnel to tilt head down while spraying and sniff gently to avoid swallowing solution.

# Intranasal Ketorolac/oral ASA protocol

**Intranasal Ketorolac and oral aspirin Challenge**

<table>
<thead>
<tr>
<th>Time</th>
<th>Intranasal Ketorolac and oral aspirin Challenge</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Day 1</strong></td>
<td></td>
</tr>
<tr>
<td>8:00 AM</td>
<td>1 spray* (1.26 mg)</td>
</tr>
<tr>
<td>8:30 AM</td>
<td>2 sprays* (1 each nostril)</td>
</tr>
<tr>
<td>9:00 AM</td>
<td>4 sprays* (2 each nostril)</td>
</tr>
<tr>
<td>9:30 AM</td>
<td>6 sprays* (3 each nostril)</td>
</tr>
<tr>
<td>10:30 AM</td>
<td>60 mg* ASA</td>
</tr>
<tr>
<td>12:00 PM</td>
<td>60 mg* ASA</td>
</tr>
<tr>
<td>3:00 PM</td>
<td>Discharge instructions</td>
</tr>
<tr>
<td><strong>DAY 2</strong></td>
<td></td>
</tr>
<tr>
<td>8:00 AM</td>
<td>150* mg</td>
</tr>
<tr>
<td>11:00 AM</td>
<td>325* mg</td>
</tr>
<tr>
<td>2:00 PM</td>
<td>Discharge instructions</td>
</tr>
</tbody>
</table>

*Clinical and objective evaluation with spirometry performed before each dose

To prepare ketorolac:
- Ketorolac 60 mg/2 ml and mix with 2.75 ml preservative-free normal saline
- Use nasal spray bottle that delivers 100 microliters/actuation
- Prime 5 sprays before use, then each spray actuates 1.26 mg ketorolac solution
- Instruct patient to tilt head down while spraying and to sniff gently to avoid swallowing solution

**Reaction Possibilities**
- Naso-ocular alone
- Naso-ocular + asthma
- Asthma only

Above may be accompanied by:
- Laryngospasm, hives, flushing, gastric pain, hypotension

**Challenge/Desensitization Outcomes**
- **Negative Challenge:** no reaction to any dose including 3 hours after 325 mg aspirin
- **Aspirin Desensitization:** after a reaction has been treated and resolved, repeat provoking dose. If no reaction: continue to escalate the dose as above
  - At 325 mg of Aspirin, desensitization is complete.
  - Discharge patient home to take 850 mg of aspirin that evening
Comparison between the protocols

Table 2. Comparison of Standard Oral Aspirin and Modified Nasal Ketorolac Timeline

<table>
<thead>
<tr>
<th>Time</th>
<th>Oral aspirin challenge</th>
<th>Intranasal ketorolac and aspirin challenge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 AM</td>
<td>20–40 mg</td>
<td>1 spray (1 in 1 nostril)</td>
</tr>
<tr>
<td>8:30 AM</td>
<td></td>
<td>2 sprays (1 in each nostril)</td>
</tr>
<tr>
<td>9 AM</td>
<td></td>
<td>4 sprays (2 in each nostril)</td>
</tr>
<tr>
<td>9:30 AM</td>
<td></td>
<td>6 sprays(^b) (3 in each nostril)</td>
</tr>
<tr>
<td>10:30 AM</td>
<td></td>
<td>60 mg of aspirin</td>
</tr>
<tr>
<td>11 AM</td>
<td>40–60 mg</td>
<td></td>
</tr>
<tr>
<td>12 noon</td>
<td></td>
<td>60 mg of aspirin</td>
</tr>
<tr>
<td>1:30 PM</td>
<td></td>
<td>Instructions and discharge</td>
</tr>
<tr>
<td>2 PM</td>
<td>60–100 mg</td>
<td></td>
</tr>
<tr>
<td>5 PM</td>
<td>Instructions and discharge</td>
<td></td>
</tr>
<tr>
<td>Day 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 AM</td>
<td>100 mg</td>
<td>150 mg</td>
</tr>
<tr>
<td>11 AM</td>
<td>160 mg</td>
<td>325 mg</td>
</tr>
<tr>
<td>2 PM</td>
<td>325 mg</td>
<td>Instructions and discharge</td>
</tr>
<tr>
<td>5 PM</td>
<td>Instructions and discharge</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) Clinical and objective evaluation performed every 30 minutes and as needed.

\(^b\) Provoking dose is repeated; symptoms are treated as indicated.
“Use of intranasal ketorolac and modified oral aspirin challenge for desensitization of aspirin-exacerbated respiratory disease”

- Intranasal ketorolac/oral aspirin group
  - 74/82 (90%) patients had provoking symptoms during ketorolac
    - 49 (66%) of these then went on to complete oral aspirin portion without symptoms
    - 25 (34%) had symptoms during oral aspirin
      - 14/25 (56%) had dominant symptom during ketorolac
      - 8/82 had symptoms only during oral portion
  - Conclude that most (63/82) had some degree of desensitization during ketorolac portion

“Use of intranasal ketorolac and modified oral aspirin challenge for desensitization of aspirin-exacerbated respiratory disease”

Table 4. Intranasal Ketorolac and Aspirin vs Oral Aspirin Challenges

<table>
<thead>
<tr>
<th>Positive for AERD</th>
<th>Intranasal ketorolac and aspirin challenge (n = 82)</th>
<th>Oral aspirin challenge (n = 92)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PNIF, mean (SD), % decrease</td>
<td>28.7 (20.3)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>FEV₁, mean (SD), % decrease</td>
<td>8.5 (12.2)</td>
<td>13.4 (12.4)</td>
<td>.01</td>
</tr>
<tr>
<td>Duration, mean (SD), d</td>
<td>1.9 (0.42)</td>
<td>2.6 (0.64)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Duration ≤2 days, No. (%)</td>
<td>68 (83)</td>
<td>18 (20)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Naso-ocular reaction only, No. (%)</td>
<td>54 (65)</td>
<td>35 (38)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

- Significant difference between protocols:
  - Mean decrease in FEV₁
  - Length of desensitization
  - Duration <2 days
  - Naso-ocular reactions only
“Use of intranasal ketorolac and modified oral aspirin challenge for desensitization of aspirin-exacerbated respiratory disease”

- Oral aspirin protocol had more extrapulmonary reactions
  - Specifically laryngospasm
  - Gastrointestinal reactions

Table 5. Types of Bronchial and Extrapulmonary Reactions

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Intranasal ketorolac and aspirin challenge, No. (%) (n = 82)</th>
<th>Oral aspirin challenge, No. (%) (n = 92)</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchial (FEV₁ ≥15%)</td>
<td>26 (32)</td>
<td>35 (38)</td>
<td>0.61</td>
</tr>
<tr>
<td>15%–19%</td>
<td>11 (13)</td>
<td>12 (13)</td>
<td>0.66</td>
</tr>
<tr>
<td>20%–29%</td>
<td>8 (10)</td>
<td>13 (14)</td>
<td>0.63</td>
</tr>
<tr>
<td>≥30%</td>
<td>7 (9)</td>
<td>10 (11)</td>
<td>0.45</td>
</tr>
<tr>
<td>Extrapulmonary reactions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laryngospasm</td>
<td>19 (23)</td>
<td>41 (45)</td>
<td>0.002</td>
</tr>
<tr>
<td>Gastrointestinal&lt;sup&gt;a&lt;/sup&gt;</td>
<td>6 (7)</td>
<td>17 (19)</td>
<td>0.02</td>
</tr>
<tr>
<td>Cutaneous&lt;sup&gt;b&lt;/sup&gt;</td>
<td>10 (12)</td>
<td>30 (33)</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>5 (6)</td>
<td>9 (10)</td>
<td>0.78</td>
</tr>
</tbody>
</table>

Abbreviations: FEV₁, forced expiratory volume in 1 second; NS, nonsignificant.
<sup>a</sup> Nausea, vomiting, gastric pain, or heartburn.
<sup>b</sup> Urticaria, angioedema, pruritus, and erythema.
“Use of intranasal ketorolac and modified oral aspirin challenge for desensitization of aspirin-exacerbated respiratory disease”

• Conclusions
  – Intranasal ketorolac/oral aspirin faster
  – Fewer extra-pulmonary reactions
  – Overall less mean decrease in FEV1

• Need to have nasal patency
  – Recent surgical polypectomy (2-4 weeks after surgery) or medical
  – Recent evaluation of degree of polyposis

• Subjectivity of naso-ocular reaction

• Silent desensitization
  – Consider repeating without LTMDs/AHs/steroids
  – Higher starting dose of ASA
Alternative Protocols

• Proposed by Aspirin Desensitization Joint Task Force
  - Smaller dosing interval (90 min vs. 2.5-3hr)
  - Fewer steps i.e. larger dose per step
  - Higher minimum FEV1
Alternative Protocols

- **Drug Allergy: An updated practice parameter, 2010**

  “The most commonly cited and tested protocol involves incremental oral administration of aspirin during 2 to 4 days, starting at 15 to 30 mg and going to 650mg. Table 12 depicts a more practical protocol; however, there are no data on the safety and efficacy of this protocol.”

<table>
<thead>
<tr>
<th>Time</th>
<th>Aspirin Dose</th>
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<tbody>
<tr>
<td>0</td>
<td>20.25 mg</td>
</tr>
<tr>
<td>90 min</td>
<td>40.5 mg</td>
</tr>
<tr>
<td>180 min</td>
<td>81 mg</td>
</tr>
<tr>
<td>270 min</td>
<td>162.5 mg</td>
</tr>
<tr>
<td>360 min</td>
<td>325 mg</td>
</tr>
</tbody>
</table>

Document informed consent and advise patient it may take several days to complete (most will take 2 days).
Establish intravenous access.
FEV₁ and clinical assessment every 90 minutes and with symptoms.
Dosing interval may be extended to 3 hours based on individual patient characteristics.
Reactions will likely occur with early doses, usually 81mg.
Treat reactions as indicated below.
After patient completely stabilized (but not less than 3 hours after the last dose), the provoking dose can be repeated.
A persistent >15% decrease in FEV₁, with or without associated symptoms, lasting longer than 3 hours despite therapy, is an indication to discontinue the desensitization process for the day.
If nasal, gastrointestinal, or cutaneous reactions occur on day 1, pretreat with histamine₁ and histamine₂ receptor antagonists for remainder of procedure.

Solensky, 2010.
Alternative Protocols

• Decrease the amount of time in between doses if asymptomatic to 90 minutes

• Retrospective review of oral challenges to aspirin, included all types of reactions to aspirin not just AERD
  – Gave ASA 30mg, 60mg, 100mg, 300mg
  – Compared 2 hr (n = 45) vs 1.5 hr (n=40) interval
  – Reduced time for positive challenge by 1 hr and negative challenge by 2 hrs
  – All reactions occurred (28/85) within 90 min
  – Concluded that likelihood of positive reaction after 90 minutes was 5.2% by time-to-event analysis
Alternative Protocols

• Increase the starting dose of aspirin
  – Review of 420 oral ASA challenge or desensitization
  – Mean provoking dose for bronchial reactions 68mg, 61 mg for naso-ocular reactions
  – 74% of reaction after 45-60mg dose

• For low risk patients consider starting existing protocol at 60mg
  – FEV1>80%, on LTMD, no ED visits for asthma, AERD >10yrs, age not 31-40
Alternative Protocols

• 1 hour dose escalation protocol
  – Patients without history of reaction ASA/NSAID sensitivity or reported reaction time to NSAIDS within 1 hour
  – Premedication regimen
  – Majority FEV1 >60% predicted

• Doses: 40, 81, 120, 162, 325mg
  – 20mg if history of intubation
  – Repeated provoking dose

• 98% of 57 desensitizations successful
  – 40% in 1 day
  – 60% in 2 days
Urgent need for ASA: cardiac event

- If need 81 mg ASA
  - Montelukast 10 mg, systemic steroid, ICS/LABA, anti-histamine
  - Split 81 mg ASA → give 40.5 mg then repeat dose in 90 minutes
    - If reacts to second dose, consider repeating 40.5mg
  - Repeat 81mg the next day

- If need to achieve 325mg
  - Administer 121.5 mg, 202.5mg, 325 mg
  - 90 minutes apart

- No data available regarding safety of protocol
Alternate Therapies for AERD

- **Xolair**
  - Adjunctive to standard therapy: patients in whom ASA desensitization not possible or failed
  - Adjunctive to ASA therapy in those failing this
  - Limited reports, n = ~5

- **Potential agents:**
  - Anti-IL5/4/13 monoclonal Ab

Gevaert, 2013; Bergmann, 2015
LAMC Outpatient AERD Challenge/Desensitization Protocol

Los Angeles Medical Center Policies and Procedures

Location: Allergy/Immunology Outpatient Clinic
Old Policy Number: 1312
On-Line Policy Number: 1312

Section: Effective Date:

Title: Review / Revision Date:
Aspirin Challenge or Desensitization for Aspirin Exacerbated Respiratory Disease (AERD)

Approved by:

PHARMACY & THERAPEUTICS COMMITTEE - 04/15
AMBULATORY POLICY COMMITTEE:
POLICY & PROCEDURE COMMITTEE - MEDICAL EXECUTIVE COMMITTEE -

Owner/Responsible Party:

Workplace Safety Key Points (WSKPs) are included in this document for your protection.
1. Always use Standard Precautions including Personal Protective Equipment (PPE) when handling any blood/body fluid, bodily fluids, and chemicals (e.g. disinfectants) or when handling spills.
2. Handwashing is the single most effective method of controlling the spread of infection, remember to always wash your hands before:
   a. Using the restroom
   b. Eating
   c. Coughing or sneezing
3. Use proper body mechanics and equipment during patient transfer and repositioning. When lifting, bend at the hips and/ or knees and keep your back straight. Ensure your work area is ergonomically correct.
4. Dispose of sharps according to policy and procedure. NO NEEDLE RECAP/PICKUP.

REFERENCES:

PURPOSE:
1. Indications for aspirin desensitization in aspirin exacerbated respiratory disease (AERD) patients 12 years of age and above
   a. Treatment of asthma and sinusitis with nasal polyps that is refractory to alternate medical management
   1) Administration of high dose aspirin improves these conditions by causing down regulation of chemical mediators/excipients/associates with AERD
   b. Indication for aspirin therapy or NSAID therapy in AERD patient for reasons other than AERD: cardiovascular, neurovascular, inflammatory conditions, pain-management
   c. Establish a diagnosis or exclude AERD.
LAMC Outpatient AERD
Challenge/Desensitization Protocol

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**B. Discuss risks, benefits, and alternatives of procedure with the patient and document in the patient’s chart:**
1. Make patient aware that in event of severe reaction, emergency department transfer and hospitalization may be necessary.

**C. Contaminations to outpatient setting:**
1. Beta-blocker use, recent myocardial infarction, other medical condition or medication that would complicate treatment of severe allergic reaction, severe asthma, and history of anaphylaxis/severe reaction to aspirin or NSAID ingestion.

**D. Patient to be seen in clinic approximately 1-2 weeks prior to procedure to ensure patient has received/or been questioned about the appropriate medications:**
1. Recent pulmonary function test showing FEV1 > 1.5L and FEV1/FVC at least 70% of patients personal best. Recent allergy and peak flow as well.
   - a. If evidence of bronchial hyperreactivity, short course of oral steroids should be considered.
2. Ensure patient received all prescribed medications for minimum of one week prior to procedure.
   - a. Consider elevation for patients determined to be at a higher risk or history of previous aspirin desensitization failures.
   - b. Discontinue beta-blockers prior to procedure.
   - c. Instruct patient whether or not to discontinue anti-histamines prior to procedure.
   - d. Challenge—generally discontinued so as not to block any signs of reaction.
   - e. Desensitization - if diagnosis of AERD shows, consultation can be made for continuation of anti-histamine during procedure.

**E. Order produced in Health Connect:**
1. See, examine, and document patient baseline on each day of desensitization prior to dosing and at end of day document summary of each day. Document patient understanding of desensitization and discharge instructions.
2. Nursing staff.
   - a. Confirm order placed by physician in Health Connect.
   - b. Schedule patient in 1:1 nursing setting for 3 consecutive days.
     - i. Patient to hold any anti-histamine for 48 hours prior to procedure and to continue all other anti-inflammation medications as instructed by prescribing allergist.
   - c. Obtain aspirin: 61 mg chewable and 325 mg.
   - d. Cut 61 mg tablets into 20 mg, 40 mg.
   - e. Ensure aspirin medications readily available in clinic.

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**LAMC Outpatient AERD Challenge/Desensitization Protocol**

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1. 30.35 mg may be omitted per discretion of allergist.
2. 45.5 mg
3. 61 mg
4. 162 mg
5. 325 mg
6. 500 mg may be omitted per discretion of allergist.
7. Additional dosing steps can be administered per discretion of prescribing allergist.

**G. Notify allergist for any concerning signs or symptoms:**
1. 15% decrease in peak flow or FEV1/FVC ordered by allergist.
2. Cough, wheezing, shortness of breath.
4. Hoarse, throat tightness, wheezing, cough, or decrease in FEV1 by 15%.
5. Trespass, tightness, difficulty breathing or swallowing.
7. Gastrintestinal pain, nausea, cramping, diarrhea.
8. Dizziness, passing out.

**H. Oral desensitizing dose is reached patient will be treated through the reaction at the discretion of the allergist and report full emancipation if appropriate:**

**I. PROVIDING DESCRIBED DOSE IS OBTAINED, AFTER 15 MINUTES WITHOUT REACTION, PROCEED WITH SUBSEQUENT DOSES OF DESCRIBED ALLERGIE:**

J. At the conclusion of Day 1:
1. Instruct patient report time for resuming the desensitization the next day.
2. Instruct patient on return precautions to emergency room for recurrence of concerning symptoms overnight (Figure 6).

K. Resolution of desensitization on Day 2:
1. Perform full set of vials, 3 peak flows, and aspirin.
2. Resume desensitization depending on results of previous day per this instructions of prescribing allergist.
3. Continue to dose every 3 hours with vials every 30 minutes.

L. Day 5/6: Complete the remaining desensitization and prepare for day 6, take aspirin at prescribed time.

M. Conclusions of desensitization:
1. Patient meet with allergist to go over further instructions and subsequent dosing.
2. Patient to receive discharge instructions (Figure 7).

N. Treatment options for treatment of reactions—be ordered by the supervising allergy MD:
   - a. Edetate 1 g every 12 hour.
   - b. Cetirizine 10 mg.
   - c. Diphenhydramine 50 mg oral.
2. Nasal:
   - a. Cetirizine — approximatively 1-2 sprays each nostril.
   - b. Chlorpheniramine 10 mg.
   - c. Diphenhydramine 50 mg.
   - d. Rhinex 0.5 g.
   - e. Omalotetrazine 1-2 sprays each nostril.
   - f. Chlorpheniramine 10 mg, diphenhydramine 50 mg, approximatively 2 sprays each nostril.
### LAMC Outpatient AERD Challenge/Desensitization Protocol

3) Laryngeal-throat tightening, difficulty swallowing, swelling, decrease in FEV1 > 15%, decrease in I2%
   a. Epinephrine IM 0.3-0.5mg
   b. Nebulized racemic epinephrine
   c. Oral/Inh antihistamines - cetirizine 10mg, diphenhydramine 50 mg
   d. Oral/Inh steroids: prednisone 10mg tablets, methylprednisolone 40mg/ml
   e. Oxygen tank and mask

4) Gastrointestinal: cramping, nausea, vomiting, diarrhea
   a. Ranitidine 150mg oral, Ranitidine 50mg IV
   b. Oral/Intramuscular antihistamines - cetirizine 10 mg, diphenhydramine 50mg
   c. Epinephrine 0.3-0.5mg

5) Pulmonary - decrease in FEV1 > 15%, shortness of breath, chest tightness, wheezing, decrease in I2%
   a. Nebulized or albuterol MDI
   b. Nebulized racemic epinephrine
   c. Oral/Inh steroids: prednisone 10 mg tablets, methylprednisolone 40mg/ml
   d. Oral/Inh antihistamines - cetirizine 10mg, diphenhydramine 50 mg
   e. Nebulized racemic epinephrine
   f. Epinephrine IM 0.3-0.5 mg
   g. Oxygen

6) Anaphylaxis/Hypotension
   a. Make sure patient supine
   b. Epinephrine 0.3-0.5mg IM
   c. IM diphenhydramine 50mg, oral cetirizine 10mg
   d. IM ranitidine 50mg
   e. Oral/Inh steroids: prednisone 10mg tablets, methylprednisolone 40mg/ml
   f. Oxygen

7) Per the discretion of the supervising allergist, the patient will be transferred to the emergency department for treatment of severe adverse reactions or for prolonged treatment outside the operational hours of the clinic.
Physician Role

• Physicians - identify appropriate patients to undergo AERD challenge/desensitization including indication for ASA/NSAID therapy and target dosing
  – Identify safety of outpatient desensitization
    • Ability to hold beta blocker for procedure, anticipated ability to withstand outpatient medical management of adverse reactions including but not limited to anaphylaxis
  – Discuss risks, benefits, and alternatives of procedure with the patient and document in the patient’s chart
    • Make patient aware that in event of severe reaction, emergency department transfer and hospitalization may be necessary.
Physician Role

– Contraindications to outpatient setting:
  • beta-blocker use, recent myocardial infarction, other medical condition or medication that would complicate treatment of severe allergic reaction, severe asthma, and history of anaphylaxis/severe reaction to aspirin or NSAID ingestion

– Patient to be seen in clinic approximately 1-2 weeks prior to procedure to ensure patient has continued/discontinued appropriate medications
  • Recent pulmonary function test showing FEV1 >1.5L and 60 % predicted and FEV1 at least 70% of patients personal best. Record average peak flow as well.
    – If evidence of bronchial hyperresponsiveness, short course of oral steroids should be considered
Physician Role

• Ensure on montelukast (or other leukotriene modifier) for minimum of one week prior to procedure
  – Consider zileuton for patients determined to be higher risk or history of previous aspirin desensitization failures
• Discontinue beta-blockers prior to procedure
• Instruct patient whether or not to discontinue anti-histamines prior to procedure
  – Challenge- generally discontinued so as to not block any signs of reaction
  – Desensitization- if diagnosis of AERD clear, consideration can be made for continuation of anti-histamine during procedure
Physician Role

– Order procedure in Health Connect
– See, examine, and document patient baseline on each day of desensitization prior to dosing and at end of day document summary of each day. Document patient understanding of desensitization and discharge instructions on dosing of aspirin therapy.

• Be present in the clinic throughout the entirety of procedure
Nurse Role

— Ensure rescue medications readily available in clinic
  • Epinephrine 1:1000 intramuscular, diphenhydramine 50mg oral and IM, methylprednisolone 40mg/mL IM, prednisone 10 mg tablets, nebulized albuterol 0.083% vials and ipratropium 0.5mg vial, nebulizer racemic epinephrine, cetirizine 10 mg, ranitidine 150 mg oral and 50mg IM, oxymetazolone, azelastine, ketotifen eye drops, oxygen

— Day of procedure- document in Health Connect
  • Perform full PFT and three peak flow maneuvers
    — Calculate numerical value for 15% decrease in FEV1 and peak flow
  • Full set of vitals including blood pressure, heart rate, and oxygen saturation
Nurse Role

- Administer aspirin as below or as per prescribing allergist every 3 hours, check full set of vitals including peak flow prior to each administration and every 30 minutes
  - 20.25 mg- may be omitted per discretion of allergist
  - 40.5 mg
  - 81 mg
  - 162 mg
  - 325 mg
  - 650 mg- may be omitted per discretion of allergist

  Additional dosing steps can be administered per discretion of prescribing allergist
LAMC Outpatient AERD Challenge/Desensitization Protocol

Los Angeles Medical Center Policies and Procedures

Los Angeles Medical Center Allergy Department
Figure B

 Overnight instruction for Aspirin desensitization for AERD

If you experience any symptoms of possible reaction overnight please do as follows:

1. Rash, hives, itching, nose congestion or sneezing, swelling outside of the mouth — please take diphenhydramine 25 mg
   a. If symptoms do not improve: please take an additional diphenhydramine 25 mg
   b. If symptoms worsen: please call the Call Center and ask to speak with the 24 hour nurse advice line (800-954-8000)
   c. In the morning, please let the nurse and Allergist know when you come in for the next day of the procedure

2. If you are having mild wheezing/shortness of breath/cough
   a. Please use your albuterol or rescue inhaler or nebulizer
   b. If not improved, please give another dose of the medication
   c. If improved, please let the nurse and Allergist know when you come in for the next day of the procedure
   d. If exacerbating, please call the Call Center and ask to speak with the 24 hour nurse advice line (800-954-8000) or for severe symptoms, please go to the emergency room or call 911
   e. Please let your Allergist know about any such reactions the next day

3. If swelling is occurring inside the mouth, throat, severe difficulty breathing/wheezing, feeling as if you are going to pass out
   a. Please go to the emergency room or call 911
   b. Please notify your Allergist’s office (800-954-8000) after you have been evaluated by the emergency room for further instructions regarding your aspirin desensitization

Medication Instructions:
Please continue to take your aspirin as directed by your allergist.
Your dose of aspirin is __________ to be taken __________

If you experience any symptoms of possible reaction in the next 24-48 hours please do as follows:

1. Rash, hives, itching, nose congestion or sneezing, swelling outside of the mouth — please take diphenhydramine 25 mg
   a. If symptoms do not improve: please take an additional diphenhydramine 25 mg
   b. If symptoms worsen: please call the 24 hour nurse advice line (800-954-8000) and please let your allergist know in the morning

2. If you are having mild wheezing/shortness of breath/cough
   a. Please use your albuterol or rescue inhaler or nebulizer
   b. If not improved, please give another dose of the medication
   c. If improved, please let the Allergist know the next day
   d. If exacerbating, please call the 24 hour nurse advice line (800-954-8000) or for severe symptoms please go to the emergency room or call 911
   e. Please let your allergist know about any such reactions the next day

3. If swelling is occurring inside the mouth, throat, severe difficulty breathing/wheezing, feeling as if you are going to pass out
   a. Please go to the emergency room or call 911
   b. Please notify your Allergist’s office (800-954-8000) after you have been evaluated by the emergency room for further instructions regarding your aspirin desensitization

Please remember to take your aspirin dose, if you miss doses you might lose your tolerance

If you miss dose:
1. If it has been less than 48 hours: continue to take your aspirin dose
2. If it has been more than 48 hours, do not take the next dose; please contact the Allergist’s office for instructions (800-954-8000)
Patient Instructions

Los Angeles Medical Center Allergy Department

Figure B

Overnight instruction for Aspirin desensitization for AERD

If you experience any symptoms of possible reaction overnight please do as follows:

1. Rash, hives, itching, nose congestion or sneezing, swelling outside of the mouth — please take diphenhydramine 25 mg
   a. If symptoms do not improve: please take an additional diphenhydramine 25mg
   b. If symptoms worsen: please call the Call Center and ask to speak with the 24 hour nurse advice line (800-954-8000)
   c. In the morning, please let the nurse and Allergist know when you come in for the next day of the procedure
2. If you are having mild wheezing/shortness of breath/cough
   a. Please use your albuterol or rescue inhaler or nebulizer
   b. If not improved, please give another dose of the medication
   c. If improved, please let the nurse and Allergist know when you come in for the next day of the procedure
   d. If worsening, please call the Call Center and ask to speak with the 24 hour nurse advice line (800-954-8000) or for severe symptoms please go to the emergency room or call 911
      i. Please let your allergist know about any such reactions the next day
3. If swelling is occurring inside the mouth, throat, severe difficulty breathing/wheezing, feeling as if you are going to pass out
   a. Please go to the emergency room or call 911
   b. Please notify your Allergist’s office (800-954-8000) after you have been evaluated by the emergency room for further instructions regarding your aspirin desensitization
Patient Instructions

Los Angeles Medical Center Allergy Department
Figure C-AERD
Post Aspirin Desensitization Patient Instructions

Medication instructions:
Please continue to take your aspirin as directed by your allergist.
Your dose of aspirin is _____, to be taken ______

If you experience any symptoms of possible reaction in the next 24-48 hours please do as follows:

1. Itch, hives, itching, nose congestion or sneezing, swelling outside of the mouth – please take diphenhydramine 25 mg
   a. If symptoms do not improve, please take an additional diphenhydramine 25 mg
   b. If symptoms worsen, please call the Call Center and ask to speak with the 24 hour nurse advice line (800-954-8000) and please let your allergist know in the morning

2. If you are having mild wheezing/shortness of breath/cough
   a. Please use your albuterol or rescue inhaler or nebulizer
   b. If not improved, please give another dose of the medication
   c. If improved, please let the Allergist know the next day
   d. If worsening, please call the Call Center and ask to speak with the 24 hour nurse advice line (800-954-8000) or if severe symptoms please go to the emergency room or call 911
   i. Please let your allergist know about any such reactions the next day

3. If swelling is occurring inside the mouth, throat, severe difficulty breathing/wheezing, feeling as if you are going to pass out
   a. Please go to the emergency room or call 911
   b. Please notify your Allergist’s office (800-954-8000) after you have been evaluated by the emergency room for further instructions regarding your aspirin desensitization

Please remember to take your aspirin daily, if you miss doses you might lose your tolerance.

If you miss a dose:

1. If it has been less than 48 hours: continue to take your aspirin dose

2. If it has been more than 48 hours: do not take the next dose, please contact the Allergist’s office for instructions (800-954-8000)
Conclusions

• Aspirin desensitization should be considered for patients with difficult to control AERD
• Desensitization for particular patients could be considered as an outpatient procedure
• LTMDs should be started prior to desensitization
• Risks of high-dose ASA therapy should be discussed with the patient and the implications of missing doses
• Adequate planning for ASA therapy and procedures
• Emerging protocols can be considered


References


References

References


Questions?
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