Allergic Rhinitis: Addressing Unmet Needs

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Allergic Rhinitis: Common Myths & Misconceptions

• Chronic nasal symptoms and headaches are just part of life
• Poorly controlled AR is not associated with serious consequences
• AR can be managed successfully with oral antihistamines alone
• INSs are frequently associated with (serious) adverse events

AR, allergic rhinitis; INS, intranasal corticosteroid.
Allergic Rhinitis: One of the Most Common Chronic Conditions in the US

• Prevalence between 10% and 30% of adults, affecting 30 to 60 million individuals in the US annually\(^1\)

• At least 25% of US households affected each year\(^2\)

• Responsible for 12.9 million office visits in 2007\(^3\)

US, United States.
What Is Allergic Rhinitis?¹

- An inflammatory disease of the upper airways, characterized by nasal congestion, sneezing, nasal itching, and rhinorrhea
- Caused by an IgE-mediated immune response to an allergen
- Classifications
  - Classified according to type of AR trigger
    - Seasonal—during a discrete time of year
    - Perennial—year round
  - Classified according to duration and severity of symptoms
    - Intermittent or persistent
    - Mild or moderate/severe

AR, allergic rhinitis; IgE, immunoglobulin E.
Allergic Rhinitis: An Inflammatory Disease

- Allergic inflammation is characterized by hyperreactivity of the nasal epithelium
- Repeated exposure to allergen elicits increasingly severe symptoms ("priming effect") and lowers the threshold for an allergic response
- Ongoing AR leads to a continuous late-phase state of mucosal eosinophilia and enhanced mediator activity
- Mediators released from eosinophils perpetuate the inflammatory cycle and lead to persistent allergic disease

AR, allergic rhinitis.
Allergic Rhinitis Is an IgE-Mediated Disease With Dual Response

1. Early-phase reaction symptoms
   - Itching
   - Sneezing
   - Rhinorrhea
   - Nasal congestion

2. Late-phase reaction symptoms
   - Nasal congestion
   - Nasal hypersensitivity
   - Rhinorrhea

IgE, immunoglobulin E; INS, intranasal corticosteroid.
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Mechanisms of Allergy: Inflammatory Cells & Mediators

APC, antigen-presenting cell; IFN, interferon; IgE, immunoglobulin E; IL, interleukin; MHC, major histocompatibility complex; TCR, T-cell receptor; TGF, transforming growth factor; TNF, tumor necrosis factor.

Allergic Rhinitis Imposes a Significant Burden on Quality of Life

- Allergy symptoms have a substantial effect on physical, social, and emotional well-being\(^1\)
  - Impaired daily activities
  - Declining health status
  - Self-image problems
  - Poorer cognitive functioning
  - Reduced work productivity
  - Increased sleep disorders

- Two surveys of patients with allergy, 4 years apart, assessed the burden of allergies in the US and its impact on QOL
  - AIA 2006\(^2\)
  - NASAL 2010\(^3\)

AIA, Allergies in America survey; NASAL, Nasal Allergy Survey Assessing Limitations; QOL, quality of life; US, United States.
Allergic Rhinitis Continues to Have a Negative Impact on Daily Life\(^1,2\)

Respondents With AR Reporting Impact of AR Symptoms on Daily Life During Worst 1-Month Period

AR, allergic rhinitis; NASAL, Nasal Allergy Survey Assessing Limitations.
2. Data can be assessed at [www.nasalsurvey.com](http://www.nasalsurvey.com).
Adults With Allergic Rhinitis Reported Their General Health Was Impaired

Self-Reported Health Status

<table>
<thead>
<tr>
<th>Health Status</th>
<th>Adults With AR (n = 116)</th>
<th>Adults Without AR (n = 406)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent</td>
<td>11</td>
<td>23</td>
</tr>
<tr>
<td>Very Good</td>
<td>29</td>
<td>31</td>
</tr>
<tr>
<td>Good</td>
<td>34</td>
<td>31</td>
</tr>
<tr>
<td>Fair</td>
<td>16</td>
<td>11</td>
</tr>
<tr>
<td>Poor</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Very Poor</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Don't Know</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

AR, allergic rhinitis.
Reprinted with permission from the *Journal of Family Practice*.1
Other Health Problems Are Reported More Frequently in Patients With Allergic Rhinitis

- Heartburn, reflux, or GERD: 36% (AR), 16% (Non-AR)
- Migraines: 9% (AR), 17% (Non-AR)
- Sleep disturbances: 9% (AR), 7% (Non-AR)
- Sleep apnea: 5% (AR), 9% (Non-AR)
- Sinusitis: 4% (AR), 12% (Non-AR)
- Skin rashes: 3% (AR), 16% (Non-AR)
- Earaches: 3% (AR), 0% (Non-AR)
- Chronic tonsillitis: 1% (AR), 0% (Non-AR)
- Conjunctivitis or red eye: 1% (AR), 5% (Non-AR)
- None of these: 29% (AR), 66% (Non-AR)

AR, allergic rhinitis; GERD, gastroesophageal reflux disease. Reprinted with permission from the Journal of Family Practice. 1

Emotional Burden of Allergic Rhinitis

Respondents With AR Reporting Impact of AR Symptoms on Emotions During Worst 1-Month Period*

*Patients who responded frequently or sometimes.

AR, allergic rhinitis; NASAL, Nasal Allergy Survey Assessing Limitations.

Reprinted with permission from the Journal of Family Practice.¹

NASAL Respondents With AR Reported Frequent Sleep Disturbances

<table>
<thead>
<tr>
<th>Problem</th>
<th>Adults With AR (n = 116)</th>
<th>Adults Without AR (n = 406)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difficulty getting to sleep*</td>
<td>24</td>
<td>8</td>
</tr>
<tr>
<td>Waking up during the night*</td>
<td>31</td>
<td>13</td>
</tr>
<tr>
<td>Lack of a good night's sleep*</td>
<td>26</td>
<td>11</td>
</tr>
</tbody>
</table>

*P < 0.05 compared with adults without AR.
† Patients who responded they were extremely or moderately troubled.
AR, allergic rhinitis; NASAL, Nasal Allergy Survey Assessing Limitations.
Reprinted with permission from the Journal of Family Practice.¹
Results from NASAL 2010 suggest that AR continues to have a substantial effect on QOL\(^1\)

- AR symptoms limit patients’ ability to participate in routine activities and lowers work productivity by ~20%
- General health is poorer in patients with AR
- Emotional burden remains high in patients with AR
- Sleep patterns are disrupted in many patients with AR

Additional effective therapies are needed to reduce the symptoms and overall disease burden of AR

AR, allergic rhinitis; NASAL, Nasal Allergy Survey Assessing Limitations; QOL, quality of life.
Treatment Options for Allergic Rhinitis

1. Environmental control
2. Specific immunotherapy
3. Pharmacotherapy
   - Intranasal corticosteroids
   - Oral and intranasal antihistamines
   - Other
     - Oral and intranasal decongestants
     - Leukotriene antagonists
     - Intranasal anticholinergics
     - Intranasal cromolyn

Management of Allergic Rhinitis: ARIA Guidelines


ARIA, Allergic Rhinitis and Its Impact on Asthma.
OTC Medications Are the Most Frequently Used Therapeutic Agents in Allergic Rhinitis

INS, intranasal corticosteroid; NASAL, Nasal Allergy Survey Assessing Limitations; OTC, over-the-counter; Rx, prescription.

Reprinted with permission from the Journal of Family Practice.

Many Patients Feel That Their Allergic Rhinitis Symptoms Are Not Well Controlled

- Not controlled at all: 3%
- Poorly controlled: 8%
- Somewhat controlled: 36%
- Well controlled: 36%
- Completely controlled: 17%

47% of patients reported their AR symptoms are not well controlled.

AR, allergic rhinitis; N = 400.
Reprinted with permission from the Journal of Family Practice.¹
No Improvement in Patient-Reported AR Symptom Control in 2010 Compared With 2006

Symptoms During Worst 1-Month Period in the Preceding Year*

- Nasal congestion: NASAL 2010 (N = 400) 56% vs. AIA 2006 (N = 2500) 60%
- Postnasal drip: NASAL 2010 (N = 400) 48% vs. AIA 2006 (N = 2500) 46%
- Repeated sneezing: NASAL 2010 (N = 400) 45% vs. AIA 2006 (N = 2500) 46%
- Watering or tearing eyes: NASAL 2010 (N = 400) 41% vs. AIA 2006 (N = 2500) 40%
- Runny nose: NASAL 2010 (N = 400) 45% vs. AIA 2006 (N = 2500) 41%
- Nasal itching: NASAL 2010 (N = 400) 35% vs. AIA 2006 (N = 2500) 31%
- Headache: NASAL 2010 (N = 400) 25% vs. AIA 2006 (N = 2500) 21%
- Facial pain or pressure: NASAL 2010 (N = 400) 21% vs. AIA 2006 (N = 2500) 18%
- Ear pain or pressure: NASAL 2010 (N = 400) 16% vs. AIA 2006 (N = 2500) 12%

*Patients who reported every or most days.

AIA, Allergies in America survey; AR, allergic rhinitis; NASAL, Nasal Allergy Survey Assessing Limitations.

Intranasal Corticosteroids

• Most effective therapy for treatment of AR because INSs treat both early- and late-phase symptoms\textsuperscript{1,2}
• Control all major symptoms: nasal congestion, sneezing, nasal itching, and rhinorrhea\textsuperscript{2}
• Similar symptom relief among INSs, despite pharmacologic differences\textsuperscript{2}
• Data from NASAL 2010 indicated that \(~\text{30\%}\) of patients with AR had used an INS in the preceding 4 weeks\textsuperscript{3}

AR, allergic rhinitis; INS, intranasal corticosteroid; NASAL, Nasal Allergy Survey Assessing Limitations.
Patients Are Less Satisfied With INSs When There Are Side Effects

*P < 0.05.

INS, intranasal corticosteroid.
1. Data can be accessed at [www.nasalsurvey.com](http://www.nasalsurvey.com).
Factors That May Reduce Adherence With INSs¹

- Efficacy
- Side effects
- Comfort
- Convenience
- Ease of use
- Cost/formulary
- Social environment

- Sensory perceptions
  - Aftertaste
  - Odor
  - Runoff
  - Nose and throat irritation

- Intensity of adverse sensory attributes is negatively correlated with patient preference for an INS and likelihood of adherence

INS, intranasal corticosteroid.
Rationale for Development of Nasal Aerosol Formulation of INS

• In 1996, 33% of patients treated with an INS used a nonaqueous aerosol formulation\(^1\)

• The Montreal Protocol called for the discontinuation of CFC-containing products, including nonaqueous nasal aerosols\(^2\)
  - During this time, only aqueous INSs were available

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CFC, chlorofluorocarbon; INS, intranasal corticosteroid.
QNASL™ (beclomethasone dipropionate) Nasal Aerosol

• Indications and Usage
  – QNASL Nasal Aerosol is indicated for the treatment of the nasal symptoms associated with seasonal and perennial allergic rhinitis in adults and adolescent patients 12 years of age and older\(^1\)
  – Uses the same formulation as QVAR® (beclomethasone dipropionate HFA) Inhalation Aerosol indicated for maintenance treatment of asthma as prophylactic therapy in patients ≥5 years old\(^2\)

• Dosage and Administration
  – The recommended dose of QNASL Nasal Aerosol is 320 µg/day administered as 2 nasal aerosol sprays in each nostril (80 µg/aerosol spray) once daily (maximum total daily dose of 4 nasal aerosol sprays/day)\(^1\)
  – QNASL Nasal Aerosol is for intranasal use only\(^1\)

1. QNASL (beclomethasone dipropionate) Nasal Aerosol Prescribing Information. Teva Respiratory, LLC; 2012.
2. QVAR (beclomethasone dipropionate HFA) Inhalation Aerosol Prescribing Information. Teva Respiratory, LLC; 2010.
Beclomethasone dipropionate (BDP) is an anti-inflammatory corticosteroid

- Prodrug, extensively converted to the active metabolite 17-beclomethasone monopropionate (17-BMP)

New nasal actuator with dose counter

1. QNASL (beclomethasone dipropionate) Nasal Aerosol Prescribing Information. Teva Respiratory, LLC; 2012.
The Parts of QNASL™ (beclomethasone dipropionate) Nasal Aerosol

Dose Counter

Canister

Protective Dust Cap

Nasal Actuator Tip

FIGURE A

FOR INTRANASAL ADMINISTRATION ONLY.

Using QNASL™ (beclomethasone dipropionate) Nasal Aerosol

1. Repeat steps E–G in the same nostril, then repeat in the other nostril.

2. Hold breath for ~5 seconds after releasing the spray.

QNASL™ (beclomethasone dipropionate) Significantly Improved rTNSS* in Patients With SAR¹,²

- At week 2, treatment difference in rTNSS with QNASL Nasal Aerosol from placebo: −0.91 (95% CI: −1.3, −0.5)
- Significant improvement in iTNSS observed with QNASL Nasal Aerosol at study end

*The rTNSS (primary efficacy endpoint) is calculated as the sum of the patients’ scoring of 4 individual nasal symptoms (rhinorrhea, sneezing, nasal congestion, and nasal itching).

• At week 2, treatment difference in rTNSS with QNASL Nasal Aerosol from placebo: −0.91 (95% CI: −1.3, −0.5)
• Significant improvement in iTNSS observed with QNASL Nasal Aerosol at study end

CI, confidence interval; i/rTNSS, instantaneous/reflective total nasal symptom score; SAR, seasonal allergic rhinitis.


2. QNASL (beclomethasone dipropionate) Nasal Aerosol Prescribing Information. Teva Respiratory, LLC; 2012.
QNASL™ (beclomethasone dipropioninate) Significantly Improved rTNSS* in Patients With PAR¹,²

Treatment Comparison Over 6 Weeks

<table>
<thead>
<tr>
<th>Change From Baseline in rTNSS</th>
<th>QNASL Nasal Aerosol 320 µg/d</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 232</td>
<td>8.9</td>
<td>9.0</td>
</tr>
<tr>
<td>N = 234</td>
<td>−2.5</td>
<td>−1.6</td>
</tr>
</tbody>
</table>

Values represent least-squares means.

P < 0.001.

Change From Baseline Over Time

- QNASL Nasal Aerosol 320 µg/d
- Placebo

P < 0.05 at all time points except day 2.

*The rTNSS (primary efficacy endpoint) is calculated as the sum of the patients’ scoring of 4 individual nasal symptoms (rhinorrhea, sneezing, nasal congestion, and nasal itching).

- At week 6, treatment difference in rTNSS with QNASL Nasal Aerosol from placebo: −0.84 (95% CI: −1.2, −0.5)
- Significant improvement in iTNSS with QNASL Nasal Aerosol at study end

CI, confidence interval; i/rTNSS, instantaneous/reflective total nasal symptom score; PAR, perennial allergic rhinitis.

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2. QNASL (beclomethasone dipropionate) Nasal Aerosol Prescribing Information. Teva Respiratory, LLC; 2012.
QNASL™ (beclomethasone dipropionate) Safety in Patients With Allergic Rhinitis\textsuperscript{1}

- In short-term trials (2–6 weeks duration) of patients with AR (N = 1394), the incidence of adverse reactions did not differ appreciably between those treated with QNASL versus placebo.

- Adverse events with ≥1% incidence and greater than placebo in QNASL 320 µg/day–treated patients:
  - Nasal discomfort (5.2%)
  - Headache (2.3%)
  - Epistaxis (1.9%)

- In the long-term trial (52 weeks duration), most adverse events were similar in type and rate between the treatment groups, except epistaxis, which was more frequent in QNASL 320 µg/day versus placebo-treated patients (11% versus 2%).

AR, allergic rhinitis.
1. QNASL (beclomethasone dipropionate) Nasal Aerosol Prescribing Information. Teva Respiratory, LLC; 2012.
Lower Systemic & Peak Exposure With QNASL™ (beclomethasone dipropionate) Versus Orally Inhaled QVAR® (beclomethasone dipropionate HFA)¹,²

- Systemic bioavailability of QNASL Nasal Aerosol 320 µg/d was ~27.5% of that of orally inhaled QVAR 320 µg/d
- Peak exposure of QNASL Nasal Aerosol 320 µg/d was ~19.5% of that of orally inhaled QVAR 320 µg/d

BMP, beclomethasone monopropionate; HFA, hydrofluoroalkane.

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2. QNASL (beclomethasone dipropionate) Nasal Aerosol Prescribing Information. Teva Respiratory, LLC; 2012.
Change in Serum Cortisol Levels After Treatment With QNASL™ (beclomethasone dipropionate) Was Comparable to Placebo in Patients With PAR\textsuperscript{1,2}

- Adolescents and adults (12 to 45 years of age)
- Similar serum cortisol concentration-time profile for QNASL Nasal Aerosol and placebo at baseline and week 6
- QNASL Nasal Aerosol noninferior to placebo
- Substantial decrease in serum cortisol concentration with prednisone

PAR, perennial allergic rhinitis.
1. Ratner PH et al. Poster presented at the Annual Meeting of the American College of Allergy, Asthma & Immunology, November 3–8, 2011, Boston, MA.
2. QNASL (beclomethasone dipropionate) Nasal Aerosol Prescribing Information. Teva Respiratory, LLC; 2012.
QNASL™ (beclomethasone dipropionate): Summary of Efficacy in Allergic Rhinitis

• Significantly greater nasal symptom relief compared with placebo in patients with SAR\(^1,2\) and PAR\(^1,3\)
  - Improvements in rTNSS and iTNSS in patients with SAR\(^2\) and PAR\(^3\)

i/rTNSS, instantaneous/reflective total nasal symptom score; PAR, perennial allergic rhinitis; SAR, seasonal allergic rhinitis.
1. QNASL (beclomethasone dipropionate) Nasal Aerosol Prescribing Information. Teva Respiratory, LLC; 2012.
QNASL™ (beclomethasone dipropionate): Summary of Safety in Allergic Rhinitis

• In short-term trials (2–6 weeks), the overall pattern of AEs with QNASL was similar to placebo

• In the 52-week long-term safety trial, most AEs were similar in type and rate between the treatment groups
  – Epistaxis occurred more frequently in patients who received QNASL (11%) than in patients who received placebo (2%)
  – No nasal septal perforations were found

• No significant HPA-axis suppression compared with placebo in adults or adolescents with PAR after 6 weeks of treatment

• Monitor growth routinely in all pediatric patients receiving corticosteroids, including QNASL

AE, adverse event; HPA, hypothalamic-pituitary-adrenal; PAR, perennial allergic rhinitis.

1. QNASL (beclomethasone dipropionate) Nasal Aerosol Prescribing Information. Teva Respiratory, LLC; 2012.
QNASL™ (beclomethasone dipropionate)
Important Safety Information¹

• Local Nasal Effects: In clinical trials up to 52 weeks, epistaxis and nasal ulcerations were observed more frequently and some epistaxis events were more severe in patients treated with QNASL Nasal Aerosol than those who received placebo. *Candida* infections of the nose, mouth, or throat may occur in patients using intranasal corticosteroids. Periodically monitor patients for signs of adverse effects on the nasal mucosa. Patients with recent nasal ulcers, nasal surgery, or nasal trauma should avoid use of QNASL Nasal Aerosol until healed.

• Glaucoma, cataracts, and increased intraocular pressure may be associated with nasal corticosteroid use.

Hypersensitivity, rash, and urticaria may occur after administration of QNASL Nasal Aerosol. Discontinue QNASL Nasal Aerosol if any such reactions occur.

Patients who have immune system problems or use drugs that suppress the immune system (e.g., corticosteroids) may be more susceptible to infections than healthy individuals. Patients may experience a more serious or even fatal course of chickenpox or measles. QNASL Nasal Aerosol should be used with caution, or not at all, in patients with existing tuberculosis; untreated fungal, bacterial, viral, or parasitic infections; or ocular herpes simplex.

• Systemic corticosteroid effects such as hypercorticism and adrenal suppression may appear if intranasal corticosteroids are used at very high dosages or at the regular dosage in susceptible individuals. If such changes occur, discontinue QNASL Nasal Aerosol slowly.

• Intranasal corticosteroids may cause a reduction in growth velocity when administered to pediatric patients. Growth of pediatric patients receiving QNASL Nasal Aerosol should be routinely monitored.

• The most common adverse reactions that may occur with QNASL Nasal Aerosol are nasal discomfort, epistaxis, and headache.
QVAR® (beclomethasone dipropionate HFA) Inhalation Aerosol Safety

QVAR (beclomethasone dipropionate HFA) Inhalation Aerosol is indicated in the maintenance treatment of asthma as prophylactic therapy in patients 5 years of age or older. QVAR is also indicated for asthma patients who require systemic corticosteroid administration, where adding QVAR may reduce or eliminate the need for systemic corticosteroids.

IMPORTANT SAFETY INFORMATION

• QVAR is not a bronchodilator and is not indicated for relief of acute bronchospasm

• Common side effects associated with the use of QVAR and placebo in clinical trials include, but are not limited to, headache (12% and 9%, respectively) and pharyngitis (8% and 4%, respectively)

• CAUTION: Adrenal insufficiency may occur when transferring patients from systemic steroids (see WARNINGS, Prescribing Information)

• A reduction in growth velocity in growing children and teenagers may occur as a result of inadequate control of chronic diseases such as asthma or from use of corticosteroids for treatment
Questions