

The Clinical Effectiveness of Aspirin Desensitization in Chronic Rhinosinusitis

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Aspirin-exacerbated respiratory disease (AERD) is a chronic inflammatory disease characterized by chronic rhinosinusitis, nasal polyposis, asthma, and airway reactivity to aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs). For patients who have inadequately controlled rhinosinusitis and/or asthma despite treatment with topical corticosteroids and leukotriene-modifying drugs, aspirin desensitization is an important therapeutic option. This review examines the evidence supporting the effectiveness of aspirin desensitization for the treatment of chronic rhinosinusitis in patients with AERD. Practical aspects of conducting safe aspirin desensitization procedures and optimizing therapeutic benefits are also reviewed. When conducted in accordance with current guidelines, aspirin desensitization is a safe procedure that allows patients with AERD who have an indication for aspirin or other NSAIDs to safely ingest these medications. There is now strong evidence that aspirin desensitization and daily aspirin therapy is effective for treatment of the chronic inflammatory disease of the upper airway and lower airways in AERD.

Introduction

Aspirin-exacerbated respiratory disease (AERD) is an acquired disorder characterized by chronic hyperplastic eosinophilic sinusitis with nasal polyposis, asthma, and airway reactivity following the ingestion of medications that inhibit the cyclooxygenase-1 (COX-1) enzyme, namely aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs). Other terms used to describe this disorder include aspirin-sensitive asthma, aspirin-induced

asthma, and aspirin hypersensitivity. Because aspirin neither initiates nor perpetuates the inflammatory disease and both the upper and lower airways are often involved, the term “AERD” is preferred [1].

The acute reaction that results from COX-1 inhibition varies in severity and typically consists of the sudden onset of rhinitis (rhinorrhea, nasal congestion, sneezing, nasal itching), bronchospasm (coughing, wheezing, dyspnea, chest tightness), and/or laryngospasm (stridor, dysphonia). These respiratory symptoms may be accompanied by extrapulmonary manifestations including conjunctivitis, urticaria, angioedema, flushing, nausea, vomiting, abdominal pain, and hypotension. Whereas the sensitivity to COX-1 inhibition can develop at any time in the progression of AERD, the chronic upper and lower respiratory manifestations generally become clinically apparent between the second and fourth decades of life. Chronic rhinosinusitis usually develops first, initially manifested as nasal congestion, followed by complaints of chronic clear or purulent nasal drainage and anosmia, and often progresses over months to years to severe hyperplastic eosinophilic sinusitis with aggressive nasal polyp formation. Asthma may preexist from childhood or may develop in adulthood, in which case it becomes apparent 2 to 5 years after the onset of the sinus disease [2].

Because of the variation in the timing and severity of each key feature of AERD, estimating the prevalence of AERD is challenging. Furthermore, many patients with the condition may not have ingested aspirin or other NSAIDs, or they may fail to correlate a mild reaction with the ingestion [3••]. A systematic review of studies designed to measure the prevalence of AERD in adults with asthma found that the prevalence was higher when determined by oral provocation testing (21%, 95% CI 14%–29%) than by patient report (3%, 95% CI 2%–4%) [4]. Older studies attempting to examine the prevalence of AERD in asthmatics with nasal polyposis estimated the prevalence to be 30% to 40% [5].

The event or series of events leading to the transformation from tolerance to intolerance of medications that inhibit COX-1 is unknown. However, it is clear that in patients with AERD, both the chronic inflammatory

respiratory disease and the acute reaction result from abnormal metabolism of arachidonic acid. Recent studies have shown that AERD is associated with overproduction of proinflammatory cysteinyl leukotrienes and prostaglandin D_2 and a relative deficiency of anti-inflammatory lipoxins and prostaglandin E_2 [6–9]. The net result is excess production of proinflammatory cytokines and recruitment of effector cells such as mast cells and eosinophils, which are capable of releasing cytotoxic molecules leading to respiratory mucosal inflammation and damage [3••]. In the acute reaction, COX-1 inhibition results in a further decrease in prostaglandin E_2 and increase in the synthesis of cysteinyl leukotrienes responsible for the acute inflammatory reaction [3••,10].

For almost 60 years after the first report by Widal et al. [11] of the successful desensitization to aspirin in a patient with what is now called AERD, the therapeutic benefit of aspirin in patients with AERD was not recognized. In 1980, Stevenson et al. [12] published a report of two patients with AERD who experienced improvement in nasal and sinus symptoms following aspirin desensitization and daily aspirin treatment for several months. In recent decades, several studies have been published demonstrating the clinical effectiveness of aspirin desensitization and treatment on the symptoms of AERD. Because recent reviews provided updates in the epidemiology, natural history, diagnostic approaches, and pathophysiology of AERD [3••,13••,14••,15,16], this review focuses on recent advances that directly relate to the clinical effectiveness of aspirin desensitization and treatment in chronic rhinosinusitis associated with AERD.

Patient Selection and Indications for Aspirin Desensitization and Treatment

Many AERD patients with chronic rhinosinusitis with nasal polyposis, asthma, and airway reactivity to aspirin and NSAIDs can be managed successfully with conventional treatments for both the upper and lower airway processes, and avoidance of medications that inhibit the COX-1 enzyme. As in patients with chronic rhinosinusitis with nasal polyposis due to other processes (eg, IgE-mediated allergic sensitization), intranasal steroids can help reduce inflammation, polyp formation, and symptoms and should be used as first-line therapy in AERD [17]. Similarly, management of asthma in patients with AERD should include inhaled corticosteroids with or without long-acting β -agonists and other therapeutic options in accordance with recently updated asthma management guidelines [18•].

Cysteinyl leukotrienes have been well established as important molecules in both the acute respiratory reaction that results from ingestion of medications that inhibit the COX-1 enzyme and the chronic inflammatory process that leads to the clinical manifestations of AERD. Thus, it is not surprising that leukotriene-modifying drugs, such

as the 5-lipoxygenase inhibitor zileuton and the cysteinyl leukotriene receptor type 1 antagonists montelukast and zafirlukast, are particularly helpful in the management of the upper and lower airway disease processes in AERD [3••,6,19–21].

Thoughtful consideration and management of additional underlying respiratory tract conditions is also important in the management of patients with AERD. Given that as many as two thirds of patients with AERD can have positive wheal-and-flare skin test responses to relevant inhaled aeroallergens [22], the importance of identifying and treating concomitant allergic inflammation cannot be overemphasized. Interventions such as allergen avoidance, antihistamines, immunotherapy, and possibly anti-IgE therapy should be considered in patients with AERD and allergic respiratory disease. Additional conditions such as infectious sinusitis and extraesophageal manifestations of acid reflux should also be considered and addressed in appropriate patients.

In general, when the symptoms of upper and/or lower respiratory disease persist despite the above interventions, or in the event of one of the following indications for treatment with aspirin or NSAIDs, consideration of aspirin desensitization followed by daily aspirin maintenance therapy is warranted [13••,14••]:

- Moderate or severe asthma and/or intractable nasal symptoms that are uncontrolled with topical corticosteroids and leukotriene-modifying drugs,
- Aggressive nasal polyp formation,
- Requirement for daily or frequent courses of systemic corticosteroids to control nasal symptoms and/or asthma,
- Additional medical indication for aspirin (eg, atherosclerotic cardiovascular disease), or
- Medical indication for other COX-1 enzyme-inhibiting medication (eg, arthritis refractory to acetaminophen).

Clinical Effectiveness of Oral Aspirin Desensitization and Treatment in AERD

The role of aspirin desensitization and daily aspirin maintenance in the management of chronic rhinosinusitis and polyposis in patients with AERD has been clearly established as a beneficial treatment (class A recommendation) that should be considered in all patients with AERD [23]. This recommendation is based on a number of clinical trials that provide strong evidence for the clinical effectiveness of aspirin desensitization in treating patients with AERD [24–32,33•].

Since the 1960s, clinicians have been performing graded oral aspirin challenges as a means of confirming the diagnosis of AERD [24,25]. In 1976, Zeiss and Lockey [26] reported their observation that a patient with asthma and

chronic rhinosinusitis with nasal polyposis who had a positive respiratory oral aspirin challenge remained refractory to the acute adverse effects of aspirin for up to 72 hours. In light of this observation, Stevenson et al. [12] conducted oral aspirin desensitization followed by an open drug trial with aspirin in two patients with AERD. They found that daily ingestion of at least 325 mg of aspirin maintained the refractory state and was associated with dramatic clinical improvement in nasal and asthma symptoms and a reduction in the requirement for systemic corticosteroids.

To confirm these initial findings, the same group conducted a randomized, double-blind, placebo-controlled, crossover study of the effectiveness of aspirin desensitization followed by daily treatment with aspirin in 25 subjects with AERD [27]. The authors found that treatment with aspirin, 325 mg, 1, 4, or 8 tablets per day for 3 months, resulted in significant improvement in nasal symptoms and reduction in nasal corticosteroid dose compared with placebo, with 75% of patients experiencing improvement. There was no significant improvement in asthma symptoms or reduction in systemic corticosteroid dose. Although this study was encouraging in that aspirin desensitization was effective to treat rhinosinusitis in AERD, the observed benefit was probably limited by underdosing of aspirin in nearly one third of subjects and the failure of the investigators to comprehensively address comorbid sinus disease.

Subsequent attempts to confirm these findings and address these limitations with blinded, placebo-controlled trials have been difficult to design. Patients enrolled in these studies report dramatic improvement in nasal congestion and a return of smell within a few days of oral aspirin desensitization, which becomes transient when treated with placebo. In addition, the availability of aspirin without a prescription precludes restriction of access to study drug in subjects taking placebo [28]. As a result, subsequent studies examining the clinical effectiveness of aspirin desensitization and treatment in AERD have utilized prospective or retrospective observational study designs. In a retrospective observational study of 107 patients with AERD, the clinical outcomes of 65 patients treated with aspirin following desensitization were compared with pretreatment baseline and 42 untreated participants who elected to avoid aspirin. Aspirin doses ranged from 325 mg, once daily to 650 mg, four times daily (mean dose, 1300 mg/d). The treatment group was followed for at least 12 months and a mean of 51 months. Aspirin-treated patients had highly statistically significant reductions from pretreatment baseline in sinus infections, nasal symptom scores, sinus operations, and systemic steroid use as compared with untreated controls. Beneficial effects were also observed in asthma parameters, including chest symptom scores, inhaled steroid use, hospitalizations, and emergency department visits, and unscheduled outpatient visits for asthma [28]. Two important caveats to this study, however, include the generally milder disease state of the control group and the observation that 46% of patients on daily aspirin maintenance

discontinued treatment, including 18% who did so because of gastrointestinal complications.

To further investigate the beneficial effect of aspirin desensitization and treatment in AERD and to address the limitations of the two previous studies, the same group examined the effects of this approach in 75 patients with AERD by comparing pretreatment and post-treatment clinical status in a number of parameters. After aspirin desensitization, patients were treated with maintenance aspirin, 325 mg daily to 650 mg three times daily (mean dose, 1214 mg/d), and followed for a mean of 3.1 years [29]. Study patients were recruited from a pool of patients referred by clinicians already optimizing comorbid sinus disease. The authors found highly statistically significant improvement in the number of sinus infections per year, hospitalizations for asthma per year, olfaction symptom scores, and doses of systemic and nasal corticosteroids.

The authors showed that aspirin desensitization and treatment was associated with a significant reduction in need for sinus surgery, including nasal polypectomy, from an average of one operation every 3 years before aspirin treatment to one operation every 10 years after aspirin treatment. The benefit of aspirin desensitization on reduced need for subsequent sinus surgery is further supported by a retrospective analysis of data collected on 15 patients with AERD undergoing functional endoscopic sinus surgery, comparing the subsequent need for revision surgery in patients who did and did not undergo aspirin desensitization and daily aspirin treatment. Although none of the 5 patients on aspirin therapy required additional surgery, 8 of the 10 patients who did not receive aspirin required additional surgery within the 24-month follow-up period [30].

Highly statistically significant improvement in rhinosinusitis and asthma was observed in another observational cohort study involving 172 patients with AERD referred for aspirin desensitization [31]. Forty-six patients (27%) discontinued aspirin treatment within 1 year for a variety of reasons, including 24 (14%) who did so for known side effects of aspirin (gastritis, gastritis with bleeding, urticaria, and epistaxis). Of the 126 patients who continued aspirin therapy (mean daily dose, 1138 mg/d) for at least a year, 87% experienced improvement in their clinical courses. Analysis of changes in clinical disease markers after 6 months and 1 year of treatment revealed significant reductions in frequency of sinus infections and sinus operations, and improved nasal and asthma symptom scores. In addition, significant reductions in the dosages of nasal, inhaled, and systemic corticosteroid were observed. A separately reported study by the same investigators demonstrated that the therapeutic benefit of aspirin desensitization and treatment on nasal symptom scores, asthma symptom scores, and systemic corticosteroid dosages is highly significant as early as 1 month after aspirin desensitization and initiation of daily aspirin treatment [32].

More recently, Lee et al. [33•] sought to compare the clinical effectiveness and risk of adverse effects of two

commonly used aspirin doses in 137 patients with AERD. Upon completion of aspirin desensitization, patients were randomized into two groups: 325 mg, twice daily or 650 mg, twice daily. After 1 month, patients taking 325 mg, twice daily were asked to increase the dose if symptoms were inadequately controlled, whereas those initially assigned to 650 mg, twice daily were asked to reduce the dose if symptoms were adequately controlled. Patients in either group could also decrease aspirin doses if side effects occurred. Patients taking 325 mg, twice daily and those taking 650 mg, twice daily at the end of 1 year had significant improvement in nasal symptom scores, asthma symptom scores, and yearly numbers of sinus infections, sinus operations, and hospitalizations for asthma as compared with baseline. In addition, systemic corticosteroid doses were decreased threefold. There was no significant difference between dosage groups in improvement of clinical disease markers or incidence of side effects.

These data from more than 500 patients with AERD provide strong evidence for a beneficial effect of aspirin desensitization followed by daily aspirin maintenance therapy on the symptoms, medication burden, and need for surgical intervention that result from the upper and lower respiratory manifestations of AERD.

Intranasal Lysine-Acetylsalicylate to Treat Nasal Polyposis Associated With AERD

Intranasally administered lysine-acetylsalicylate (LAS) has also been investigated as a treatment for nasal polyposis in patients with AERD [34–36]. An early study evaluating the effectiveness of intranasal LAS after surgical polypectomy in 28 “aspirin-intolerant” patients with nasal polyposis demonstrated a significantly reduced risk of nasal polyposis relapse at 24 months compared with untreated controls (32% vs 81%, $P < 0.0001$) [34]. A small, double-blind, placebo-controlled, crossover trial failed to demonstrate significant improvement in clinical outcomes in LAS-treated AERD patients as compared with placebo [35]. A recent open, uncontrolled study in 13 patients with AERD and nasal polyposis found a reduction in polyp size on nasoendoscopic examination but no improvement in nasal symptoms [36].

In summary, some evidence exists that intranasal LAS is effective to treat nasal polyposis in AERD. However, the effectiveness of LAS seems limited to a beneficial effect on nasal polyp formation. Whether this modality is effective for reduction in nasal symptoms or in the lower respiratory disease associated with AERD requires further study.

Practical Clinical Aspects of Aspirin Desensitization

Despite strong evidence for a beneficial effect of oral aspirin desensitization and treatment on the chronic upper and lower respiratory manifestations of AERD, this approach

is underused [13••,24,37]. The syndrome of AERD and the benefits of aspirin therapy are often unrecognized among patients and even many physicians. Almost invariably, the diagnostic possibility of AERD is not considered until an episode of lower respiratory symptoms is provoked by ingestion of aspirin or another NSAID. Even when the possibility of AERD is recognized, the availability of centers with adequate interest, experience, and resources capable of performing aspirin challenges and desensitizations may be limited. Fortunately, the accumulation of experience in thousands of patients has helped reduce the actual and perceived barriers to appropriate use of aspirin desensitization therapy in AERD. Table 1 presents a summary of measures that should be considered to enhance safety and effectiveness of aspirin desensitization.

Predesensitization preparation

Table 2 lists important prechallenge/desensitization procedures aimed at simultaneously optimizing the diagnostic sensitivity and the safety of aspirin challenge and desensitization [13••,14••]. Spirometric assessment at least 1 week before challenge allows time for appropriate interventions to optimize pulmonary function and minimize risk of severe aspirin-induced bronchospasm, such as with increasing doses of inhaled corticosteroids or adding inhaled long-acting β -agonists or oral corticosteroids. In addition, the protective benefit of leukotriene-modifying drugs on aspirin-induced bronchospasm in the setting of aspirin desensitization has been established by two large-scale retrospective studies [38,39•]. Thus, we recommend initiating montelukast, 10 mg, once or twice daily for at least 1 week before desensitization. Because antihistamines and decongestants may mask the signs and symptoms of a positive aspirin challenge, withholding these agents is recommended. For situations in which transient discontinuation of these agents would be poorly tolerated and the prechallenge probability of AERD is sufficiently high, aspirin challenge/desensitization can still be performed. If an acute aspirin-provoked respiratory reaction is not observed in this setting, the possibility of a masked reaction should be considered. Given the observation that a clinical benefit of aspirin can be observed as early as 1 month after initiation of aspirin [32], empiric aspirin maintenance and close observation for clinical improvement after at least 1 month is recommended.

An additional consideration in preparation for aspirin desensitization is timing in relation to sinonasal surgery. Ideally, patients with chronic hyperplastic sinus disease and/or nasal polyposis should undergo aspirin desensitization after sinus surgery. It has been our observation that aspirin therapy is not effective at reducing existing hyperplasia or polyps, but is particularly effective at preventing or retarding regrowth.

Traditionally, the majority of aspirin desensitization procedures have been performed in hospital settings with immediate access to an intensive care unit. In fact, all the

Table 1. Optimizing safety and clinical effectiveness of aspirin desensitization and treatment for rhinosinusitis in AERD

Enhancing safety	Management
1. Pretreatment	Montelukast, 10 mg daily Appropriate ICS/LABA If necessary, oral corticosteroid
2. Ensure stable asthma	FEV ₁ > 60% and variability < 10%
3. Desensitization protocol precautions	IV line in place Monitoring hourly and with symptoms Early and aggressive treatment of reactions
Enhancing effectiveness	
1. Patient selection	Refractory symptoms despite treatment Aggressive nasal polyp formation Need for systemic corticosteroids
2. Predesensitization sinus surgery	As indicated
3. Continued use of topical steroids and LTMDs	As indicated
4. Appropriate aspirin dose	Start 650 mg BID, may be reduced to 325 mg BID
5. Promote adherence and side effects management	Provide anticipatory guidance for management of: Gastrointestinal complications Perioperative aspirin dosing Need for brief interruption of therapy
6. Treat concomitant conditions	Allergic rhinitis and/or asthma Allergen avoidance Immunotherapy Anti-IgE therapy Acid reflux Lifestyle modification Proton pump inhibitors Infectious sinusitis Antibiotics
AERD—aspirin-exacerbated respiratory disease; BID—twice daily; FEV ₁ —forced expiratory volume in 1 second; ICS—inhaled corticosteroids; IgE—immunoglobulin E; IV—intravenous; LABA—long-acting β -agonist; LTMD—leukotriene-modifying drug.	

aspirin desensitization procedures analyzed in the above studies from our institution supporting the effectiveness of aspirin desensitization and treatment were performed in the inpatient setting of a general clinical research center [27–29,31,32,33•]. However, it has recently become clear that in most patients, aspirin desensitization can be performed safely in the outpatient setting over two to three 8-hour days [14••] (Table 1). Since February 1, 2005, all aspirin desensitizations at our institution have been safely and successfully performed in the outpatient setting, in a total of 102 patients (Stevenson DD, unpublished data).

Challenge and desensitization procedure

In patients with suspected AERD who have not undergone a confirmatory graded aspirin challenge, the first phase of the procedure could be considered a graded chal-

lenge that is followed immediately by desensitization. The protocol utilized for aspirin challenge and desensitization at our institution begins with 30 to 60 mg followed by 100 mg, 150 mg, and 325 mg. For convenience at centers without access to a compounding pharmacy, fractions of 81-mg then 325-mg aspirin tablets can be used, beginning with 20.25 mg or 40.5 mg followed by 60.75 mg, 81 mg, 101.25 mg, 162.5 mg, and 325 mg. Because reactions to aspirin, 650 mg, in the desensitization setting have not been observed, patients can take this dose the following day. Whereas a recent practice paper [14••] suggests that subsequent doses can be given every 90 minutes, the mean time to reaction following a dose of aspirin is 102 minutes (Hope AP and Stevenson DD, unpublished data). As a result, a 3-hour interval between doses may optimize patient safety. Patients should be closely monitored with

Table 2. Preparation for aspirin challenge and desensitization: to be initiated 5 to 7 days before procedure

Intervention	Goal
1. Assess airway stability with spirometry	FEV ₁ > 60% predicted, > 70% patient's personal best, or > 1.5 L FEV ₁ hourly x 3 hours with < 10% variability
2. Pretreat	Montelukast, 10 mg once to twice daily Ensure appropriate treatment for level of asthma control or severity, including inhaled corticosteroids and/or long-acting β -agonists (if indicated) [18•] Continue oral corticosteroids (if necessary to control asthma) Consider course of oral corticosteroids to achieve optimal FEV ₁
3. Eliminate "masking" agents	Discontinue oral, nasal, or ocular antihistamines and decongestants
FEV ₁ —forced expiratory volume in 1 second.	

clinical assessment and forced expiratory volume in 1 minute every hour and with any symptoms.

The dose immediately preceding the reaction is considered the provoking dose and is most commonly between 30 and 100 mg, with most patients reacting following the 60-mg dose. The type and severity of aspirin-induced reactions vary. A recent analysis of 210 patients with suspected AERD who underwent aspirin challenge/desensitization found that naso-ocular reactions occurred in 90% and bronchial/laryngeal reactions in 43%. Extrarespiratory reactions were also noted, with gastrointestinal reactions occurring in 23% and cutaneous reactions in 10% [40]. Reactions should be treated early and aggressively, as indicated. Inhaled or nebulized β -agonists should be used to treat bronchial reactions, nebulized racemic epinephrine for laryngeal reactions, topical antihistamine/mast cell stabilizers for ocular reactions, and oral or topical antihistamines/decongestants for nasal reactions. Aspirin-induced urticaria, angioedema, and flushing should be treated with intravenous or oral antihistamines. Nausea, vomiting, and abdominal cramping are usually very responsive to intravenous or oral H₂-antihistamines. It should be noted that generally, the extrarespiratory reactions to aspirin do not recur with continued maintenance aspirin therapy.

Once the reaction manifestations have been stabilized and after at least 3 hours, the provoking dose should be repeated and subsequent reactions appropriately treated before proceeding with higher doses. Because three doses (each separated by 3-hour intervals) can usually be given per day, the full desensitization procedure could be expected to take 2 to 3 days.

Aspirin maintenance

In light of the results of the study by Lee et al. [33•] designed to identify the optimal dose selection for daily aspirin treatment, we recommend a starting aspirin dose of 650 mg, twice daily (beginning the morning after desensitization) for the first month. For patients with adequate symptom response, systemic corticosteroids should be reduced or eliminated, and if symptom responses are sustained, the aspirin dose could then be reduced to 325 mg, twice daily. If breakthrough symptoms recur, resuming aspirin, 650 mg, twice daily would be appropriate.

One important barrier to success of maintenance aspirin therapy for chronic rhinosinusitis associated with AERD is discontinuation of aspirin. In studies with greater than 12 months of follow-up, total aspirin discontinuation rates ranged from 13% to 46%, with 6% to 18% of patients discontinuing aspirin due to gastrointestinal complications (dyspepsia, abdominal pain, gastritis, or intestinal bleeding) [27–29,31,33•]. Other reasons for discontinuation of aspirin therapy included lack of improvement in respiratory symptoms, rash, planned surgery, and epistaxis. Physicians involved in the care of patients with AERD should play an active role in providing education and guidance when the question of the need to discontinue aspirin arises. In the case of gastrointestinal side effects, risks and benefits of continuing aspirin therapy should be considered. Because proton-pump inhibitors have been shown to reduce dyspepsia and allow healing of peptic ulcers in patients requiring ongoing therapy with NSAIDs, a trial of daily proton-pump inhibitors may be helpful for patients wishing to continue aspirin therapy despite mild symptoms [41].

Because of the depletion of cellular stores and de novo synthesis of many of the proinflammatory mediators that occur during aspirin desensitization, a 48- to 72-hour refractory period follows aspirin desensitization and is maintained by continued administration of aspirin [26]. As a result, resumption of aspirin therapy after a brief interruption (< 48 hours) due to illness or surgery is considered safe. If aspirin therapy with at least 325 mg per day is interrupted for longer than 48 hours, repeat desensitization is recommended [14••].

Conclusions

Current evidence provides strong support for the clinical effectiveness of aspirin desensitization and treatment in AERD patients with chronic rhinosinusitis in terms of reduced nasal symptoms, chest symptoms, need for surgical intervention, and medication burden. The collective experience of those actively involved in the management of AERD has identified several factors likely to optimize the safety and clinical effectiveness of this therapeutic approach (Table 1). However, numerous real and perceived barriers to more widespread use of aspirin therapy remain. With greater awareness of AERD and the effec-

tiveness of aspirin as a therapeutic option, and greater availability of centers capable of providing regional leadership in the management of this condition, more patients can be successfully managed.

Disclosures

No potential conflicts of interest relevant to this article were reported.

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