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ORIGINAL ARTICLE

# The role of aspirin desensitization in patients with aspirin-exacerbated respiratory disease (AERD)☆

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**KEYWORDS**
Desensitization immunological;
Aspirin;
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Nasal polyps

**Abstract**
*Introduction:* Aspirin-exacerbated respiratory disease (AERD) consists of a classic tetrad: moderate/severe asthma, chronic rhinosinusitis, nasal polyps, and intolerance to aspirin or other nonsteroidal anti-inflammatory drugs. Clinical control with drugs, surgery, and desensitization are treatment options.
*Objective:* To evaluate the efficacy and tolerability of aspirin desensitization in patients with AERD.
*Methods:* Periodic symptom assessment and endoscopy in patients with AERD undergoing surgery who were desensitized.
*Results:* Seventeen patients were desensitized. Eight patients completed the desensitization and were followed for a minimum of a one-year period (mean 3.1 years). These patients showed improvement in all symptoms. Moreover, surgical reassessment was not indicated in any of these patients and there was a decrease in costs with medication and procedures. Eight patients did not complete desensitization, mainly due to procedure intolerance and uncontrolled asthma, whereas another patient was lost to follow-up.
*Conclusion:* Aspirin desensitization, when tolerated, was effective in patients with AERD and with poor clinical/surgical response.


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**PALAVRAS-CHAVE**
Dessensibilização imunológica;
Aspirina;
Sinusite;
Polipose nasal

**O papel da dessensibilização à aspirina em pacientes portadores de doença respiratória exacerbada por aspirina (DREA)**

**Resumo**
*Introdução:* A doença respiratória exacerbada por aspirina é composta pela tétrade clássica: asma moderada/grave, rinossinusite crônica, pólipos nasais e intolerância à aspirina ou outro anti-inflamatório não esteroide. Controle clínico com medicamentos, cirurgias e dessensibilização são opções de tratamento.
*Objetivo:* Avaliar a eficácia e tolerabilidade da dessensibilização à aspirina em pacientes com doença exacerbada por aspirina.
*Método:* Avaliação periódica dos sintomas e exame endoscópico em pacientes com doença respiratória exacerbada por aspirina submetidos à cirurgia e dessensibilizados.
*Resultados:* Dezessete pacientes foram dessensibilizados, dos quais oito pacientes completaram a dessensibilização e foram acompanhados pelo tempo mínimo de 1 ano (média de 3,1 anos). Todos referiram melhora de todos os sintomas; não houve nenhuma indicação de reabordagem cirúrgica, e houve redução de gastos com medicações e procedimentos. Outros oito pacientes não completaram a dessensibilização, principalmente por intolerância ao procedimento e descontrole da asma, enquanto outro paciente perdeu o seguimento.
*Conclusão:* A dessensibilização à aspirina, quando tolerada, mostrou-se eficaz nos pacientes com doença respiratória exacerbada por aspirina com resposta clínica/cirúrgica insatisfatória.


## Introduction

Aspirin-exacerbated respiratory disease (AERD), also described in the literature as Samter's triad and aspirin-induced asthma (AIA), is a clinical syndrome whose symptoms are induced by a non-allergic hypersensitivity reaction, independent of IgE,[1–5] to aspirin and/or other non-steroidal anti-inflammatory drugs (NSAIDs), cyclooxygenase-1 (COX-1) enzyme inhibitors. It was originally described by Widal et al.[6] in 1922 and by Samter and Beer[7] in 1967. The classical presentation comprises the tetrad: moderate to severe asthma, chronic hypertrophic eosinophilic rhinosinusitis, sinonasal polyps, and intolerance to aspirin or other NSAIDs.[1]

Symptom onset usually occurs in adulthood, usually before the age of 40,[1,3] and the number of affected women is higher than that of men.[1,2] There is no described association with ethnicity and family history is rarely present.[3] Studies show that its prevalence in the general population is 0.3%–0.9%, reaching 10%–20% in patients with asthma, affecting 30%–40% of asthmatics with nasal polyposis and chronic rhinosinusitis.[1,3]

The physiopathology of AERD is not fully known. The first theory, proposed by Szczeklik in 1988, associated a viral respiratory infection as a trigger for AERD.[4] More recent studies have shown the release of cytokines *in vitro* by lymphocytes infected with respiratory syncytial virus, parainfluenza virus, and rhinovirus. Cytokines recruit, stimulate, and activate inflammatory cells.[4,5]

Another factor appears to be the increased expression of specific cytokines associated with activation and survival of eosinophils in nasal polyps, such as interleukin 5 (IL-5), GM-CSF (granulocyte-macrophage colony-stimulating factor), and eotaxin, which would increase the intensity of local eosinophilic inflammation.

It is believed that patients with AERD have genetic polymorphisms that lead to reduced activity of the COX-1 isoenzyme and increased affinity of leukotriene receptors, with low production of PGE2 (prostaglandin E2) and low COX-2 expression in nasal polyps. Since PGE2 has anti-inflammatory activity, the inhibition of eosinophil chemotaxis and its activation, and a decreased production of this prostaglandin (PG) would contribute to the development of more severe eosinophilic inflammation. These alterations in the arachidonic acid metabolism lead to an imbalance in the PG/leukotriene ratio in these patients, causing inflammatory alterations in the upper and lower airways.[8–11]

The ingestion of aspirin (acetylsalicylic acid) or NSAIDs by a sensitive patient inhibits COX-1 and results in the exacerbation of the inflammation already present in the upper and lower airways, with a wide spectrum of severity and manifestations that range from conjunctivitis and rhinitis to laryngospasm and bronchospasm.[1] Initially, the clinical manifestation of AERD is nasal congestion, which may be reported by the patient as an upper-airway viral infection that never resolved. Hyposmia or anosmia occurs in most patients with AERD.[3] This rhinitis develops into chronic hypertrophic eosinophilic pansinusitis and emergence of nasal polyps, which recur even after surgical excision. Asthma may already be present from childhood or young adulthood, or occur after three months to five years of symptom onset, and is usually moderate to severe. Hypersensitivity skin tests are usually negative in patients with AERD, indicating higher prevalence in non-atopic individuals.[12]