IMMUNOTHERAPY
(RHINOLOGY POINT OF VIEW)

Rhinology Round
Afrah Alshala R3
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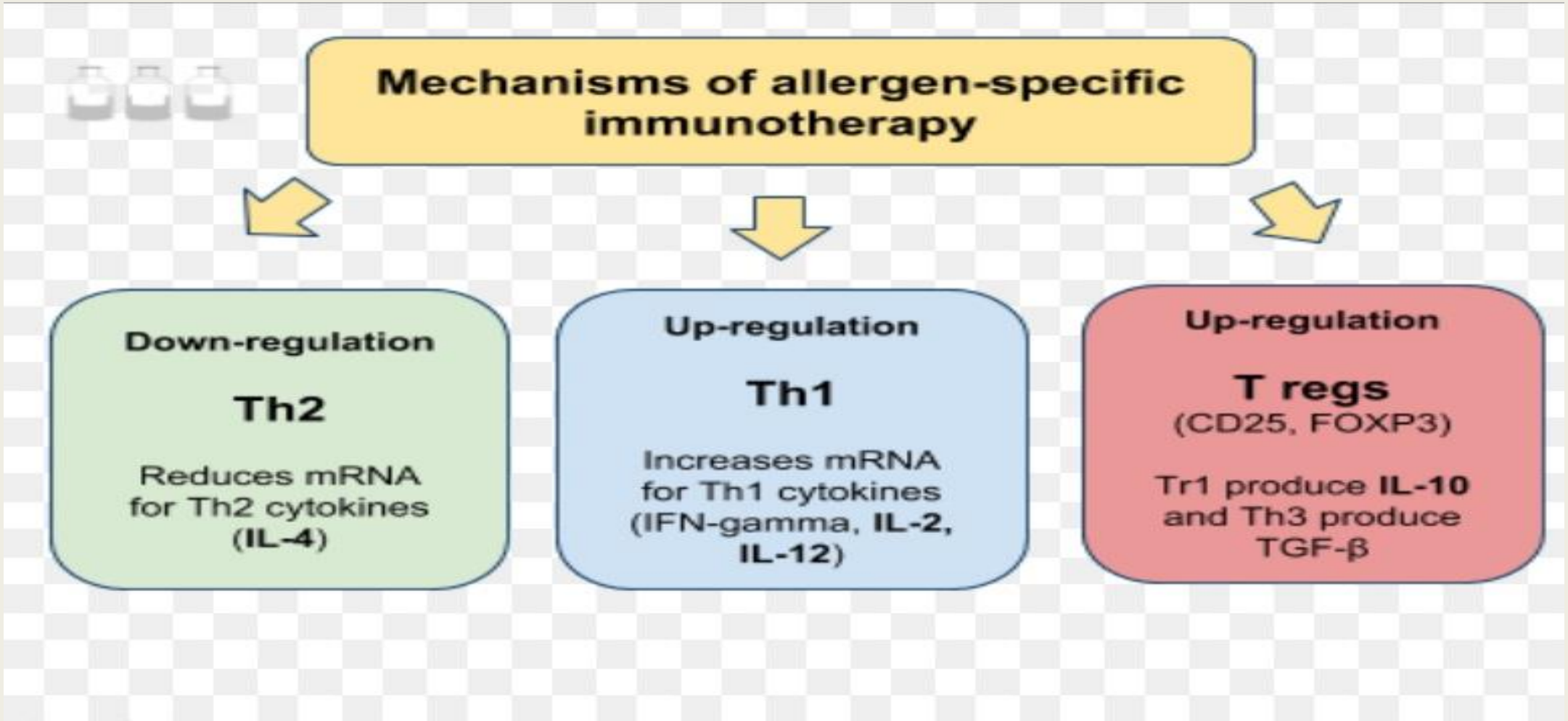
Objectives

- **Definition**
- **Mechanism of action**
- **Indications of IT**
- **Contraindications of IT**
- **IT and AR**
- **IT and AFS**
- **IT and CRS**
- **Other ENT applications of IT**

Definition

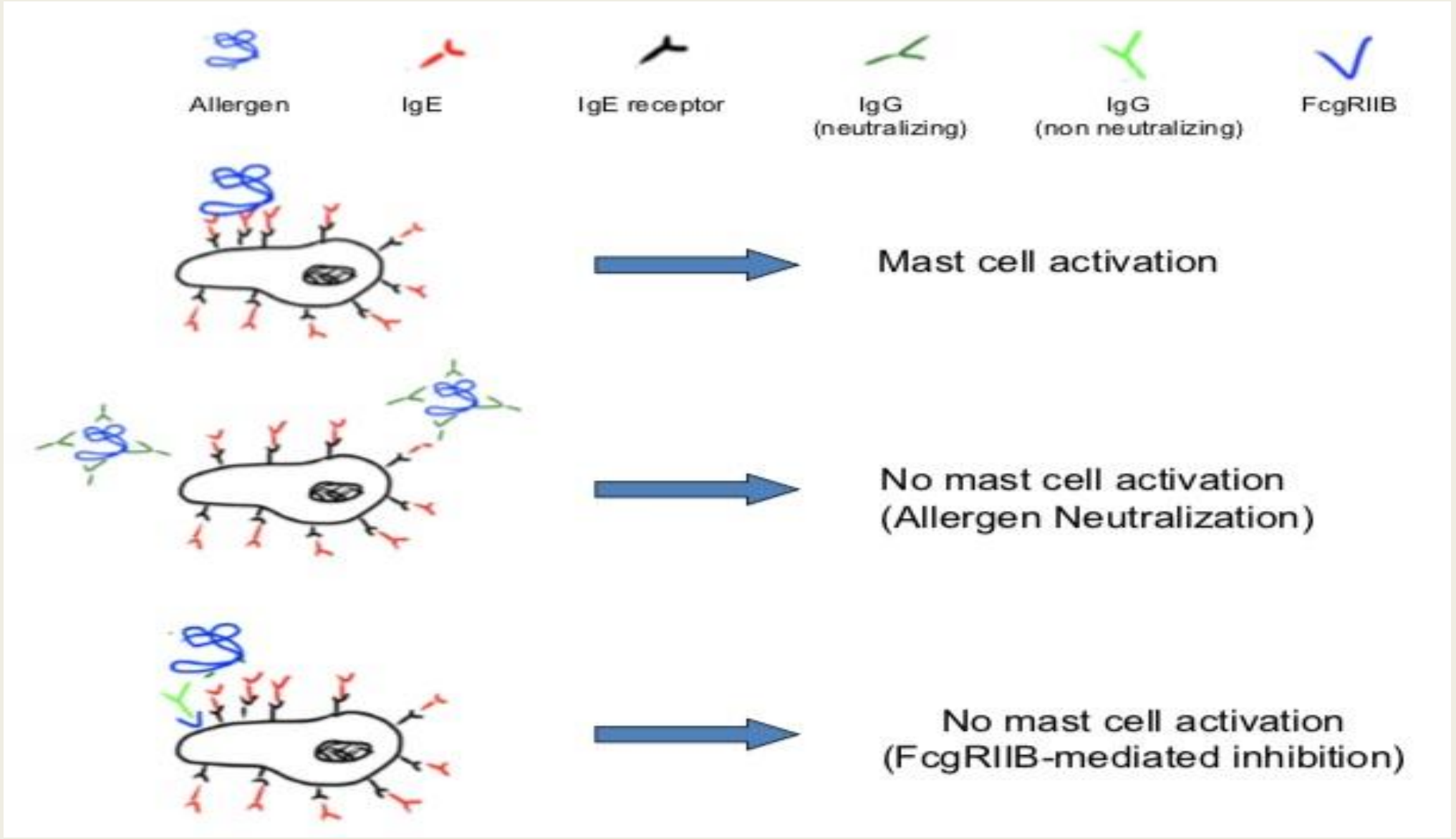
repeated administration of specific allergens to patients with IgE-mediated allergies for the purpose of providing protection against the allergic and inflammatory reactions associated with natural exposure to the same allergens

Effect of immunotherapy



b. Other observed immunologic effects :

- Initial rise in specific IgE levels, with suppression in specific IgE levels over time with treatment
- Increase in specific IgG4 levels for treated allergens


Allergen
IgE
IgE receptor
IgG
(neutralizing)
IgG
(non neutralizing)
FcgRIIB
Mast cell activation
No mast cell activation
(Allergen Neutralization)
No mast cell activation
(FcgRIIB-mediated inhibition)

General indications

AIT should be considered when all of these criteria are met:

-Symptoms strongly suggestive of AR, with or without conjunctivitis

-There is evidence of IgE sensitization (positive SPT and/or

serum-specific IgE) to one or more clinically relevant allergen

-Moderate-to-severe symptoms which interfere with usual

daily activities or sleep despite regular and appropriate pharmacotherapy and/or avoidance strategies

- AIT may also be considered in less severe AR where a patient wishes to take advantage of its long-term effect on AR and potential to prevent asthma with grass pollen AIT

Absolute contraindications

- Uncontrolled or severe asthma .
- Active, systemic autoimmune disorders (unresponsive to treatment) .
- Active malignant neoplasm .
- Immunotherapy initiation during pregnancy .

Relative contraindications

- Partially controlled asthma
- Beta-blocker therapy (local or systemic)
- Severe cardiovascular diseases, for example, coronary artery disease
- Systemic autoimmune disorders in remission or organ specific

- Severe psychiatric disorders
- Poor adherence
- Primary and secondary Immunodeficiencies
- History of serious systemic reactions to AIT

Immunotherapy and AR

- Immunotherapy (IT) has been well established as an effective treatment for AR.
- inducing up-regulation of regulatory T cells and antigen-specific IgG, while decreasing antigen-specific IgE.
- Together, this dampens the immune response to offending antigens and decreases nasal inflammation.

Immunotherapy for allergic fungal sinusitis

- The current management of AFS includes surgery, maintenance of adequate sinus drainage, and following surgery, treatment will typically include sinus irrigation with saline, and intranasal or systemic corticosteroids .

- allergy immunotherapy (AIT) has become an important therapeutic adjunct to the treatment of AFS.

REVIEW

Immunotherapy for allergic fungal sinusitis

Ashley G. Hall and Richard D. deShazo

Purpose of review

Allergic fungal sinusitis (AFS) results from an immunoglobulin E (IgE)-mediated, eosinophil-predominant hypersensitivity reaction to extramucosal fungi within the paranasal sinuses. Although the pathogenesis of this noninvasive process is still not fully understood, there is new information. Recently, the use of allergen immunotherapy with fungal antigens as an adjunct in treatment of AFS has been evaluated. In this review, we summarize the experience in the published literature on the topic.

- a retrospective review of seven patients with AFS who received allergen immunotherapy noted that five patients who received fungal immunotherapy prior to the recognition and surgical removal of allergic mucin had no improvement or an exacerbation of symptoms
- The other two patients, who had previous adequate surgical management first, improved with immunotherapy.

- a case report described the use of immunotherapy in a patient with Bipolaris AFS .
- After failing treatment with nasal steroids, antibiotics, nasal polypectomies, and several surgical procedures, the patient was started on Bipolaris immunotherapy.
- After 18 months of immunotherapy with fungal extract, symptoms and polyposis resolved along with a significant improvement

Immunotherapy for allergic fungal sinusitis

Ashley G. Hall and Richard D. deShazo

- Mabry In his first study on nine patients treated postoperatively,
- the formation of nasal crusts and reaccumulation of allergic mucin stopped within 12 weeks of starting immunotherapy.
- Systemic corticosteroid was not needed after 2 months of immunotherapy,
- and topical steroid requirement was reduced .
- In a follow-up after 13–25 months of immunotherapy, two patients had required revision surgery
- and one still required nasal saline irrigation and topical nasal steroids.
- The remaining seven patients were symptom-free and required no special care or medications

- In another study of 11 patients, after 1–3 years of immunotherapy, none had required frequent treatment with brief courses of systemic steroids,
- and only 3 were receiving topical nasal steroids.
- No repeat surgeries for recurrent AFS had been required

Immunotherapy for allergic fungal sinusitis

Ashley G. Hall and Richard D. deShazo

- Mabry et al. published a retrospective comparison of two groups of patients with AFS treated with similar regimens except for immunotherapy.
- There was significant improvement in quality-of-life scores (P<0.002) and endoscopic mucosal staging (P<0.001) in the 11 patients receiving immunotherapy after a mean of 33 months.
- In addition, immunotherapy was shown to reduce reliance on systemic (P<0.001) and topical nasal (P<0.043) corticosteroid therapy to control disease.
- All 11 members of the control group required an average of two courses of systemic corticosteroids per year, whereas the treatment group required none.

- One small series addressed the optimal duration of immunotherapy in patients with AFS .
- After at least 3 years of treatment with immunotherapy in eight patients, No evidence of recurrent polyp disease or accumulation of allergic mucin or fungal crusts was seen on exam 7–17 months after immunotherapy.

Table 1. Summary of studies involving patients with AFS treated with fungal immunotherapy

Study	Number of AFS patients treated with immunotherapy	Average duration of treatment	Main result
Ferguson [20]	7	Unknown	5 patients with no improvement or exacerbation of disease, 2 patients with improvement in symptoms
Quinn *et al.* [11]	1	18 months	Improvement in symptoms
Mabry *et al.* [13]	9	8.6 months	Decreased need for oral and topical corticosteroids
Mabry and Mabry [14]	10	20 months	2 patients required revision surgery, 1 patient was on nasal irrigation, 7 patients symptom free
Mabry *et al.* [15]	11	28 months	No revision surgeries, 3 patients on topical nasal steroids
Folker *et al.* [17]	11	33 months	Improvement in quality-of-life scores and endoscopic mucosal staging, reduced systemic and topical nasal corticosteroids
Bassichis *et al.* [18]	36	Unknown	Decreased number of office visits requiring any intervention
Marple *et al.* [19]	10	Unknown	No significant impact in the number of operations, sinonasal mucosa staging, and quality-of-life scores but overall doing well
Mabry *et al.* [16]	8	40 months	No recurrence of disease after 7–17 months off immunotherapy
Greenhaw *et al.* [21▪▪]	14	21.8 months	No adverse reactions in patients with AFS other than those which may occur with pollen immunotherapy

- COMPLICATIONS OF ALLERGEN IMMUNOTHERAPY IN ALLERGIC FUNGAL SINUSITIS :

- In the seven studies by Mabry and colleagues there were no reports in these studies to suggest that there were any serious short or long-term untoward reactions . no systemic, severe local, or immune complex reactions were reported.

- In a study of the clinical features of AFS by another group, fungal immunotherapy was administered to 11 of 20 patients. Only 4 of 11 were adherent to the prescribed regimen. Similarly, no complications were mentioned.

- These data demonstrate that fungal immunotherapy in patients with AFS is unlikely to cause adverse reactions other than those which may occur with pollen immunotherapy

Outcomes after discontinuing immunotherapy for allergic fungal sinusitis

RICHARD L. MABRY, MD, BRADLEY F. MARPLE, MD, and CYNTHIA S. MABRY, RN, C ORLN, Dallas, Texas

- eight patients with AFS had received a course of immunotherapy of at least 3 years' duration .
- They had been off injections for 7 to 17 months .
- None of the 8 patients examined had any evidence of recurrent polyp disease or accumulation of allergic mucin or fungal crusts after discontinuing immunotherapy.
- One patient required steroids for asthma but not for sinus disease.
- Four patients reported a need to irrigate at least 2 or 3 times weekly to prevent nasal crusting , whereas the other 4 no longer irrigated their sinuses.

Fungal immunotherapy in patients with allergic fungal sinusitis

- Objective: To determine the safety of high-dose subcutaneous fungal immunotherapy in patients with allergic fungal sinusitis.
- Methods: assessed in 14 patients with AFS . Results were compared to a control group of 14 patients with CRS without AFS who received subcutaneous fungal immunotherapy.

Fungal immunotherapy in patients with allergic fungal sinusitis

- Because allergic fungal sinusitis is a chronic inflammatory reaction to fungi within the sinuses, there is reason for concern that the administration of concentrated fungal allergens in immunotherapy could be associated with untoward events.
- In this study, they found no evidence that reactions to fungal immunotherapy were associated with more frequent or more severe reactions in patients with AFS than CRS patient without AFS .

Immunotherapy and CRS

Systematic review of immunotherapy for chronic rhinosinusitis

Kristen DeYoung, B.S.,[1] Jennifer L. Wentzel, M.S.,[1] Rodney J. Schlosser, M.D.,[1,2]
Shaun A. Nguyen, M.D., M.A.,[1] and Zachary M. Soler, M.D., M.Sc.[1]

- The goal of this publication is to systematically review the literature regarding effect of IT in patients with atopic CRS. including without polyp, with polyp, and allergic fungal rhinosinusitis subgroups
- Seven studies met the inclusion and exclusion criteria for this review.

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- **Symptom Scores :**
- Asakura et al. found that the children receiving subcutaneous IT had significant improvements in sneezing, rhinorrhea, and nasal obstruction after 2–3 months of treatment (p 0.01),
- whereas the otherwise medically managed atopic control group only improved in sneezing (p 0.05).

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- Schlenter et al. came to similar conclusions by comparing symptom score measurement.
- At 4 months, the IT group had less severe symptoms than the atopic controls.
- At the long-term follow-up point, the IT group continued to experience an improvement in symptoms

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- **Endoscopic Exam :**
- Turbinate hypertrophy was estimated during the endoscopic exam of atopic children with CRS after 2–3 months with or without IT treatment. Hypertrophy was significantly reduced in the IT treatment group after treatment but unchanged in the control group

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- Middle meatus closure and synechiae formation were assessed .
- at an average of 14 months of follow-up , Middle meatus closure was observed in 5 of 66 patients using IT and 1 of 6 atopic controls,
- and synechiae formation was seen in 8 of 66 IT patients and 1 of 6 controls.
- The small sample size of the control group limited the usefulness of statistical analysis.

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- **Polyp Recurrence and Need for Revision Surgery:**
- Polyp recurrence rates were reported by a singular study
- Twelve of the 34 patients (35.3%) receiving IT had a recurrence in polyps in 13/58 operative sides (22.4%)
- when compared with 2 of 5 (40%) non-IT patients in 4/8 sides (50%).
- The small sample size of the control group limited the usefulness of statistical analysis.

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- **Average Number of CRS-Related Office Visits**
- One retrospective chart review reported the average number of office visits for sinus complaints in patients with AFRS.
- Overall, there was a significant difference in yearly office visits for sinusitis management between a group of 36 patients who had received IT and a control group (n 24) treated without it.

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- **CONCLUSION**

- This study found weak evidence supporting IT as a specific treatment to improve symptoms and clinical measures of CRS when used as an adjunct to traditional therapies, primarily in the postoperative period, with available studies having major limitations.

Other ENT applications of immunotherapy

- Otitis Media with effusion .
- Eosinophilic Otitis Media .
- Meniere’s Disease .
- Eosinophilic Esophagitis .
- Malignancies .

- Immunotherapy can be a viable option for unlimited condition . The key point is understanding the pathophysiology at both molecular and cellular level .

THANK YOU