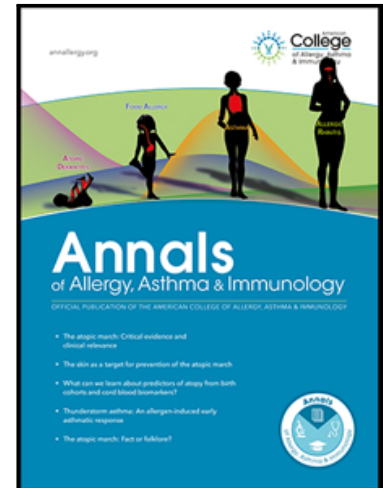


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## When medical treatments fail: Surgical interventions for allergic rhinitis

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The current recommendations for the diagnosis, assessment, and treatment of rhinitis were recently published.<sup>1</sup> These guidelines include a detailed algorithm for severe persistent symptoms of allergic rhinitis (AR), ultimately recommending that if there is a very severe presentation and/or if severe mucosal “edema” is still present even after the patient has received comprehensive medical therapies (antihistamines, intranasal corticosteroids, intranasal anticholinergics, and/or oral decongestants) then at that point an oral corticosteroid (CCS) burst would be warranted. But no further recommendations are provided in this algorithm, the implication being that this CCS burst will provide the ultimate beneficial response and subsequently the patients can go back to the “usual” medical therapies and enjoy a favorable remission.

But is that premise true? Corticosteroids are particularly effective at eliminating obstruction associated with vascular leakage and the inflammation associated with engagement of an eosinophilic process. However, CCS are less effective or fully ineffective at reversing other pathologies associated with airflow obstruction. Remodeling of the *lower* airway certainly occurs with severe inflammation and many asthmatics develop irreversible – corticosteroid resistant – obstruction. This remodeling includes epithelial shedding, goblet cell hyperplasia, basement membrane thickening, sub-epithelial fibrosis, airway smooth muscle hyperplasia and increased angiogenesis.<sup>2</sup> This extensive remodeling has not been considered to occur in the upper airway – but is that conclusion appropriate? No remodeling changes comparable to what is observed in the lower airway have been reported in the upper airway, but this merely reflects the surprising absence of any well performed study exploring the pathological basis for refractory inferior turbinate hypertrophy in AR.<sup>2</sup> But perhaps it is worth questioning whether the nasal obstruction produced by severe turbinate hypertrophy or, as will be discussed below,

central compartment atopic disease, will resolve after a course of oral CCS or, alternatively, whether AR, similar to asthma, can occasionally evolve into a steroid-refractory state.

Surgical interventions aimed at allergic rhinitis primarily focus on *inferior turbinate reduction* and interruption of *posterior nasal nerve* (and, more historically, *vidian neurectomy*). While the nasal septum may exhibit baseline deviation contributing to obstruction, addressing the structural abnormalities does not specifically address the pathogenic component of AR. The inferior turbinate anatomy consists of a bony concha, submucosal tissue and mucosal lining with serous and mucous glands. Within these layers of highly vascular mucosa are venous sinusoids, smooth muscle that is under autonomic control, and this glandular tissue, all of which can become robustly hypertrophic in various degrees, and that together at some point can become unresponsive to medication.<sup>4-5</sup> In addition to the failure of the usual AR interventions, medically-refractory congestion and tissue remodeling should be strongly considered when anterior rhinoscopy performed before and after application of a topical decongestant continues to display significant turbinate swelling (figure 1A).

Many surgical interventions currently exist – the details of which are beyond the scope of this paper – to address the underlying turbinate hypertrophy while limiting the damage to the surface epithelium and preserving long-term mucociliary clearance. These include, but are not limited to, inferior turbinate outfracture, partial surgical turbinectomy and various forms of microdebrider, radiofrequency, laser, thermal, and coblation-powered inferior turbinate reductions.<sup>4-5</sup> No specific surgical intervention has been demonstrated to provide clear superior benefit based upon randomized control trials. However, when appropriately applied, these techniques have demonstrated improvement in nasal obstruction along with decreased reliance on medical treatment without the historic concerns of empty nose syndrome/atrophic rhinitis.

Another consideration for the surgical treatment of chronic rhinitis, although more frequently utilized with non-allergic rhinitis, is interruption of the parasympathetic innervation of the nasal mucosal. Current surgical techniques include focused posterior neurectomy while in-office cryoablation and temperature-controlled radio-frequency procedures have evolved that seek to alter the autonomic input to the mucosal tissue under local anesthesia.<sup>5</sup>

A more recently described cause of refractory nasal obstruction is central compartment atopic disease (CCAD). In 2017, DelGaudio *et al.* defined the term CCAD for when there are findings of polypoid changes present on both nasal endoscopy and radiographic imaging involving the central compartments of the nasal cavity, that is hypertrophic changes involving the middle and superior turbinates and the posterior superior nasal septum.<sup>3</sup> A typical CT appearance is displayed in figure 1B.

CCAD is a presentation of severe aeroallergen sensitization that is refractory to medical therapy including intranasal and oral antihistamines, immunotherapy, and intranasal as well as *systemic* CCS. Although studies are lacking, CCAD may display remodeling changes similar to those observed in the lower airways of asthmatics. Management of these patients generally requires surgical intervention, including endoscopic sculpting of the central compartment to open up the nasal cavity and affected sinuses.<sup>3</sup> Following surgery continued nasal CCS need to be employed along with consideration for IT to prevent recurrences.

As noted above, virtually nothing is known regarding the pathological basis for refractory inferior turbinate hypertrophy or CCAD. However, it is plausible that goblet cell and acinar gland hypertrophy, immune cell infiltration, matrix deposition, and other putative manifestations of upper airway remodeling could respond to one or more of the biologics available for severe

asthma. If this could be accomplished with only a brief intervention, a short course of biologics could be a cost effective alternative to surgery.

In summary, while not generally considered to be a manifestation of allergic rhinitis, similar to asthma, it is increasingly apparent that severe, persistent upper airway inflammation can produce a myriad of remodeling changes, including especially combinations of smooth muscle hypertrophy and, most importantly, hyperplasia of the venous sinusoids and both serous and mucous glands. In contrast to the “acute” inflammatory changes associated with IgE/mast cell hypersensitivity that synergizes with the inflammation associated with eosinophilic and other immune cells, these remodeling changes are refractory to currently utilized medical interventions. The evolution of refractory inferior turbinate hypertrophy or central compartment atopic disease should be suspected when the disease becomes refractory to all medical interventions – including a reasonable course of systemic CCS. As an important source of the negative impact of AR on our patient’s quality-of-life, surgical intervention for refractory obstruction should be considered. This is especially important to appreciate given the utilization of novel interventions focusing on submucosal resection that, in contrast to historic use of complete turbinate resection, are not associated with development of empty nose syndrome or persistent atrophic rhinitis.

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## Figure Legend:

Figure 1: Refractory nasal obstruction in allergic rhinitis. 1A. Severe middle turbinate hypertrophy is suggested when middle turbinate swelling is present before (left) and largely persists after application of topical oxymetazoline (right). 1B. Central compartment atopic disease. CCAD is suggested by CT scan demonstrating robust hyperplasia of nasal mucosa and anterior ethmoid tissue along with the relative sparing of the maxillary (and other) sinuses

