

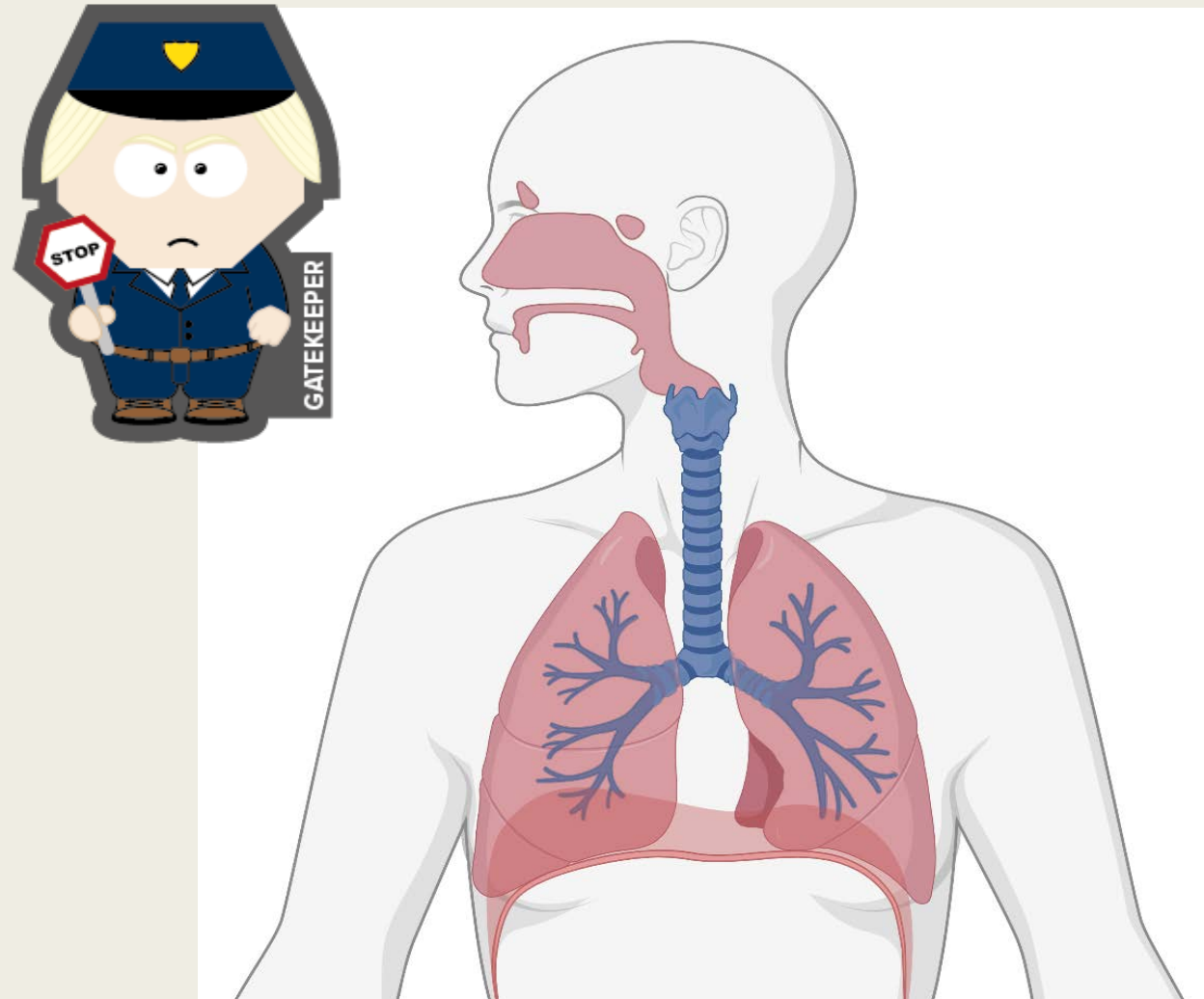
# NON-ALLERGIC RHINITIS

*Abeforcal 2021*

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IREC Pole Pulmonology/ORL/Dermatology, UCLouvain  
Brussels, Belgium

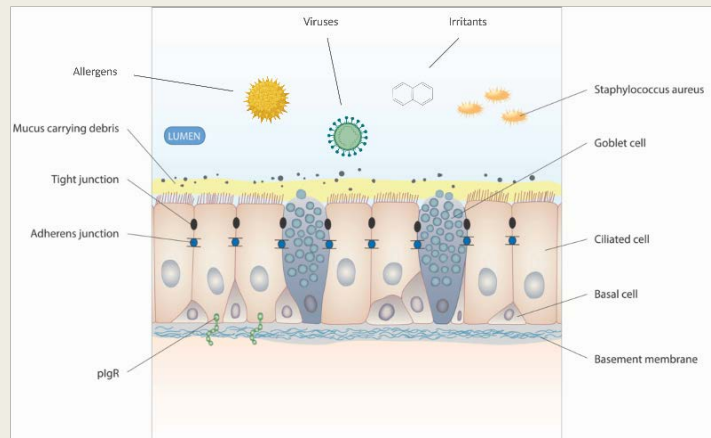
# Nose = gatekeeper of the airways



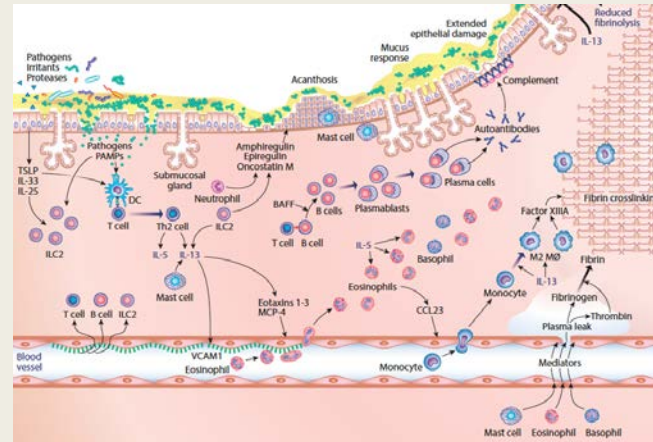


# Nose = gatekeeper of the airways

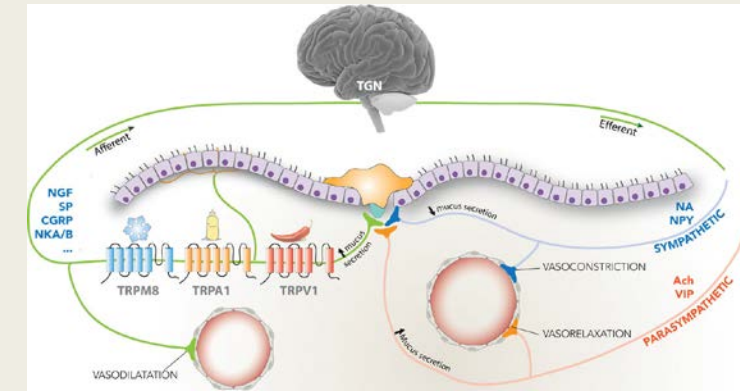
## Epithelial barrier



## Innate and adaptive immune system



## Neurovascular system



If 1 of these systems fails → Rhinitis

# Rhinitis



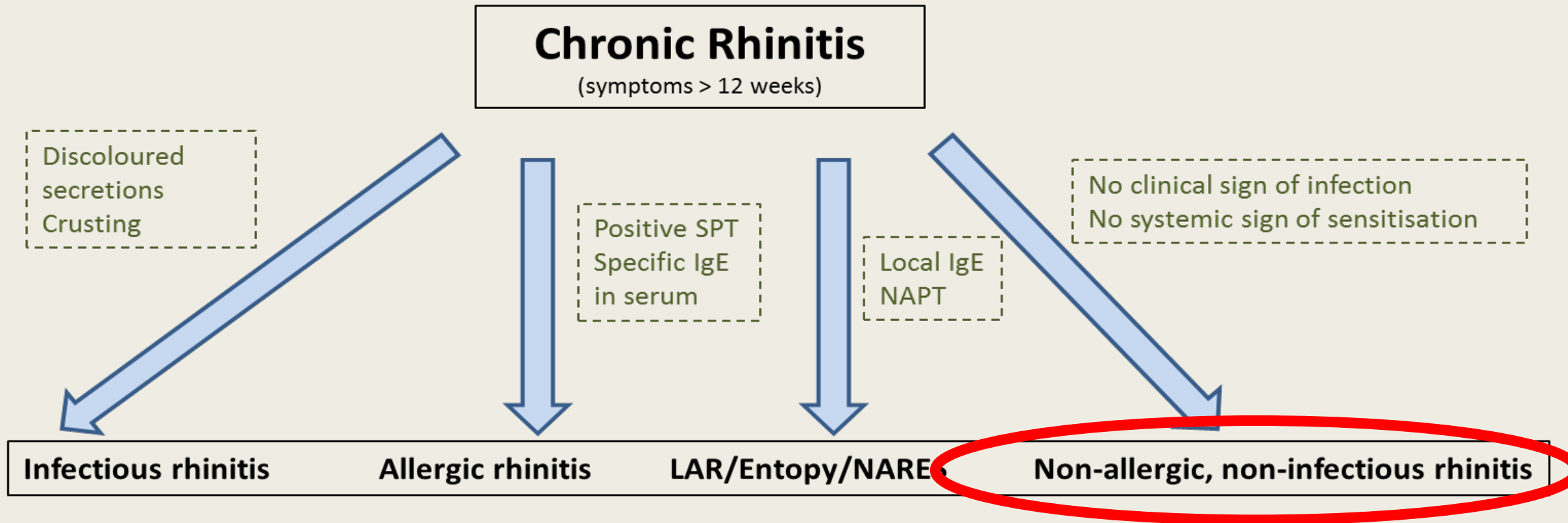
= symptomatic inflammation of the nasal mucosa, leading to at least 2 of the following symptoms:

- *Nasal obstruction*
- *Rhinorrhea*
- *Sneezing*
- *Itch*

→ Chronic rhinitis = Symptoms >12 weeks for >1h/day on most days

**Prevalence: 20-30% population!**

# Chronic Rhinitis



# Non-allergic rhinitis (NAR): Differential Diagnosis

## ■ Allergic Rhinitis:

- = typical symptoms that correlate with test results!!
- Mixed rhinitis?

## ■ Infectious Rhinitis:

- Viruses cause common colds = **acute** rhinitis.
- 0.5- 2 % → bacterial superinfection: leading to **sinusitis**.
- Nasal **vestibulitis**: infection of vestibular skin with *S. Aureus*

## ■ Rhinosinusitis:

- Rhinitis symptoms + Facial pressure and/or smell loss
- + CT changes and/or endoscopic findings

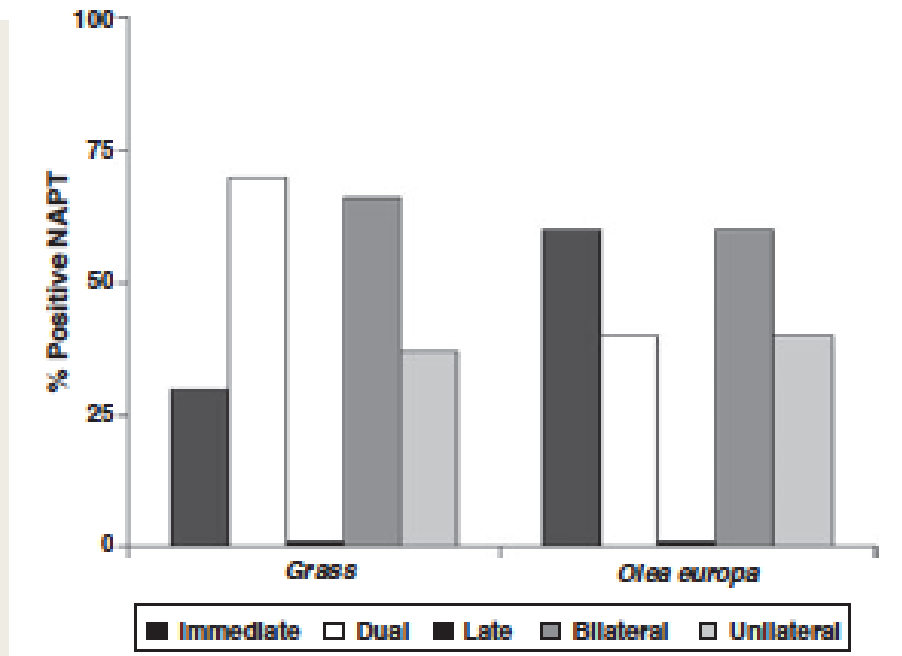


# Local Allergic Rhinitis

## Local allergic rhinitis: Concept, pathophysiology, and management

Carmen Rondón, MD, PhD,<sup>a</sup> Paloma Campo, MD, PhD,<sup>a</sup> Alkis Togias, MD, PhD,<sup>b</sup> Wytske J. Fokkens, MD, PhD,<sup>c</sup> Stephen R. Durham, MD, PhD,<sup>d</sup> Desmond G. Powe, PhD,<sup>e</sup> Joaquim Mullol, MD, PhD,<sup>f</sup> and Miguel Blanca, MD, PhD<sup>a</sup> *Málaga and Barcelona, Spain, Bethesda, Md, Amsterdam, The Netherlands, and London and Nottingham, United Kingdom*

- NO systemic allergen-specific IgEs (negative SPT- and serum test)
- BUT positive nasal provocation test with the suspected allergen
- +/- local allergen-specific IgEs in nasal secretions



Rondon et al. JACI 2008

→ Prevalence and spontaneous evolution are largely unclear!



# Chronic Rhinitis

(symptoms > 12 weeks)

Discoloured secretions  
Crusting

Positive SPT  
Specific IgE  
in serum

Local IgE  
NAPT

No clinical sign of infection  
No systemic sign of sensitisation

Infectious rhinitis      Allergic rhinitis      LAR/Entopy/NARES      Non-allergic, non-infectious rhinitis

- Gustatory rhinitis
- Occupational rhinitis
- Hormonal-induced rhinitis
- Drug-induced rhinitis

Patient history

Per exclusionem

**Idiopathic rhinitis (50%)**





# Idiopathic Rhinitis (IR)

= diagnosis per exclusionem.

- **Prevalence?** (problem terminology: vasomotor, intrinsic rhinitis ...)  
Estimated to be 50 % van NAR

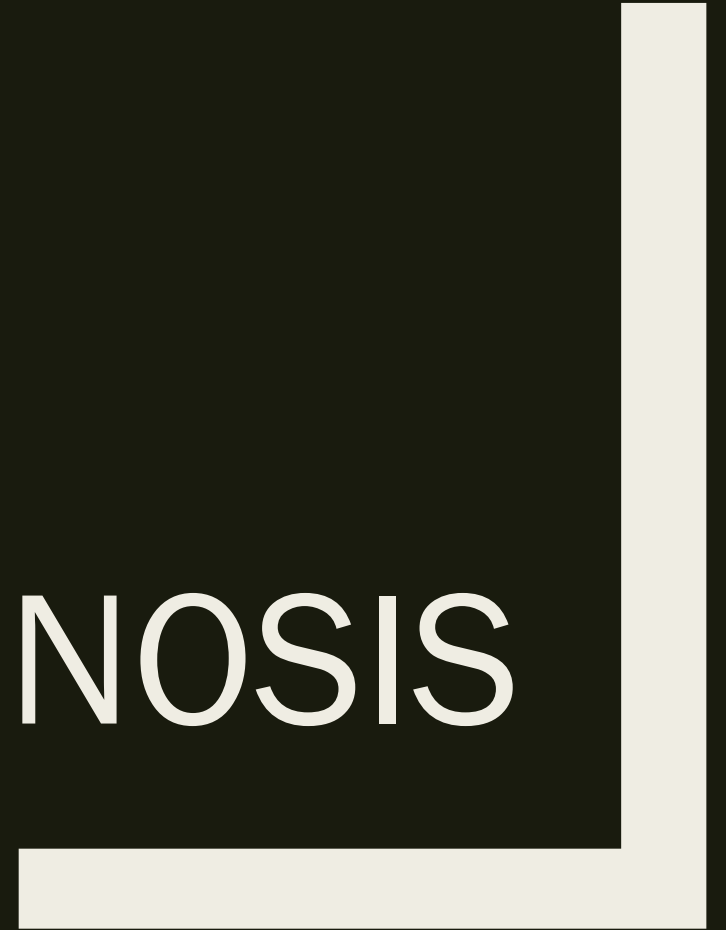
- Majority presents with **Nasal Hyperreactivity (NHR)**

= Increased sensitivity of the upper airways to 'unspecifieke triggers', which leads to rhinitis symptoms (rhinorrhea, nasal obstruction, sneezing, itch)

- *Physical triggers: changement in temperature/humidity, spicy food*
- *Chemical triggers: tobacco smoke, cleaning products, exhaust fumes, perfumes, chlorine, ...*



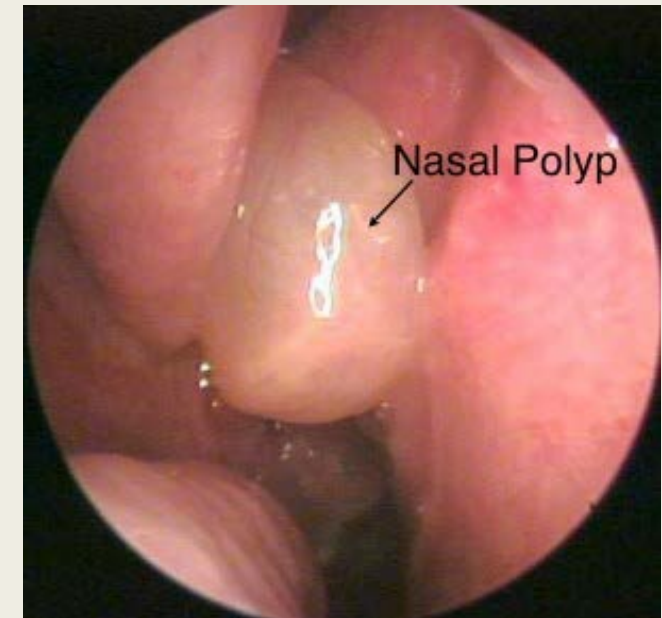
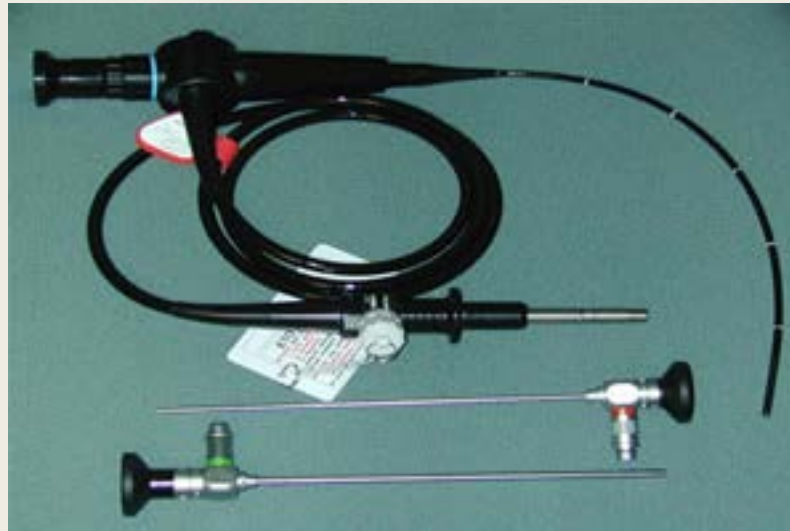
DIAGNOSIS



# History !

- *Type/duration of symptoms*
- *triggers for symptoms*
- *medication use*
- *comorbidities*
- *exposures at work/hobbies*
- *colleagues with symptoms*
- *smoking*
- *...*

# Clinical rhinological examination



# Nasal provocation testing

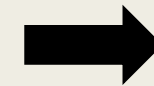
- **Specific:** *Local Allergic Rhinitis, Occupational rhinitis*

POSITION PAPER

WILEY **Allergy** EUROPEAN JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY EAACI

**EAACI Position paper on the standardization of nasal allergen challenges**

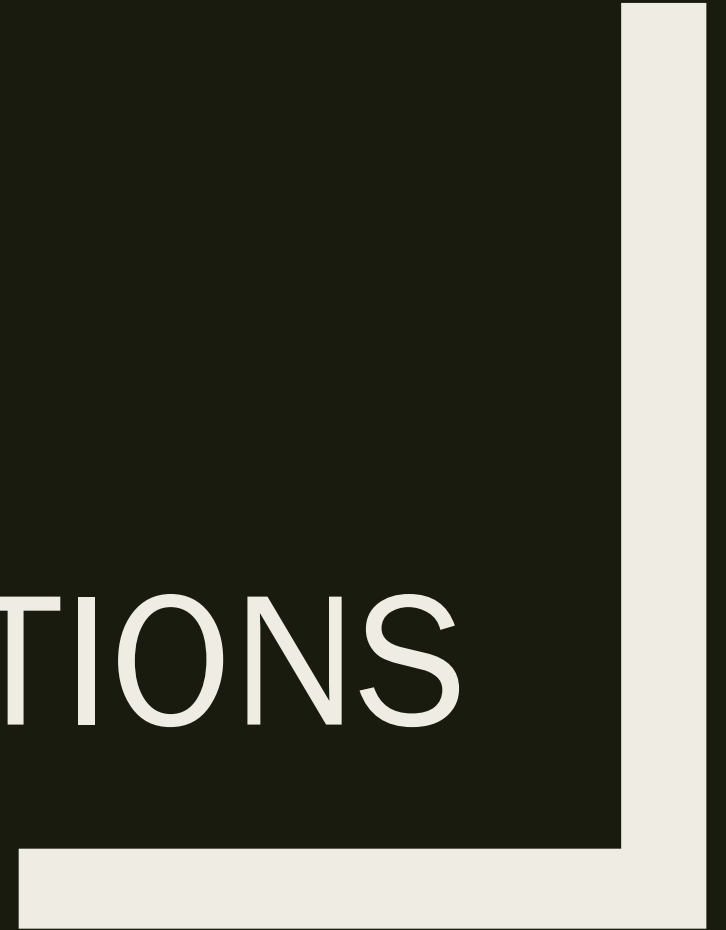
- **Unspecific:** *Nasal Hyperreactivity: Cold Dry Air*



Drop of 20% after  
15' of CDA (-10C)  
exposure

*Van Gerven et al, Laryngoscope 2012*

# TREATMENT OPTIONS



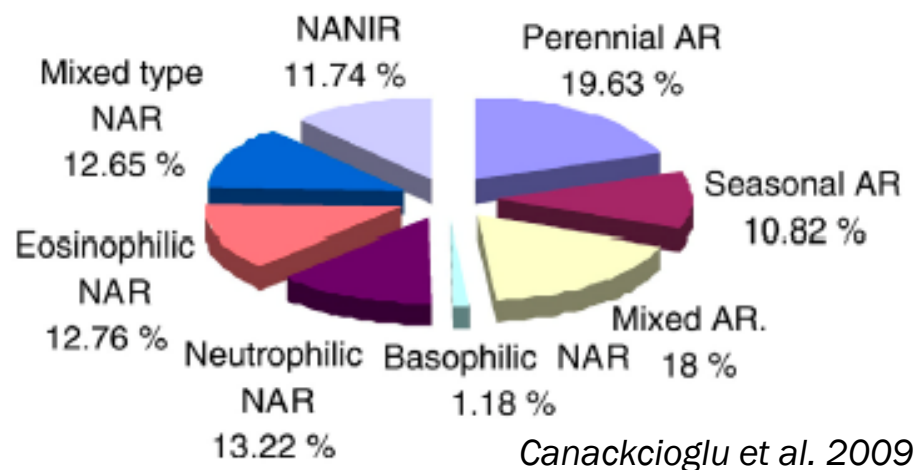
# Treatment Options

- **Treatment of underlying disease:**  
systemic disease/vasculitis, hormonal imbalances
- **Trigger Avoidance**
  - *Specific: Occupational Rhinitis, Drug-induced Rhinitis*
  - *Unspecific: Nasal Hyperreactivity (Idiopathic AND other forms rhinitis)*
- **Nasal saline douching**
  - *Active placebo!*
  - *Occupational Rhinitis and other forms*

# Nasal Steroids

## ■ Active in case of inflammatory pathology!

- Local Allergic Rhinitis
- Some forms of occupational rhinitis (allergens, LMW sensitizers)
- Auto-immune diseases / Vasculitis
- Idiopathic Rhinitis ??



## Effectiveness of Nasal Steroids in IR

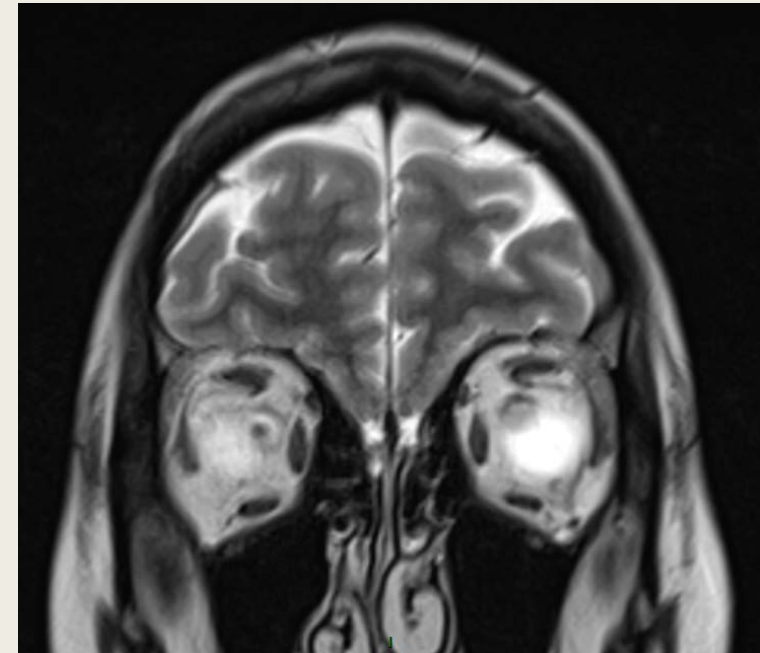
YES	NO
<i>Dockhorn et al. 1999</i>	<i>Blom et al. 1997</i>
<i>Lundblad et al. 2001</i>	
<i>Webb et al. 2002</i>	





# What if nasal steroids fail ?

1. Wrong use of spray ?
2. Wrong diagnosis ?





# What if nasal steroids fail ?

1. Wrong use of spray ?
2. Wrong diagnosis ?
3. Non-inflammatory pathology?

**Table 1** Ultrastructural and immunoelectron microscopic findings in patients with AR, IR, and of the control group

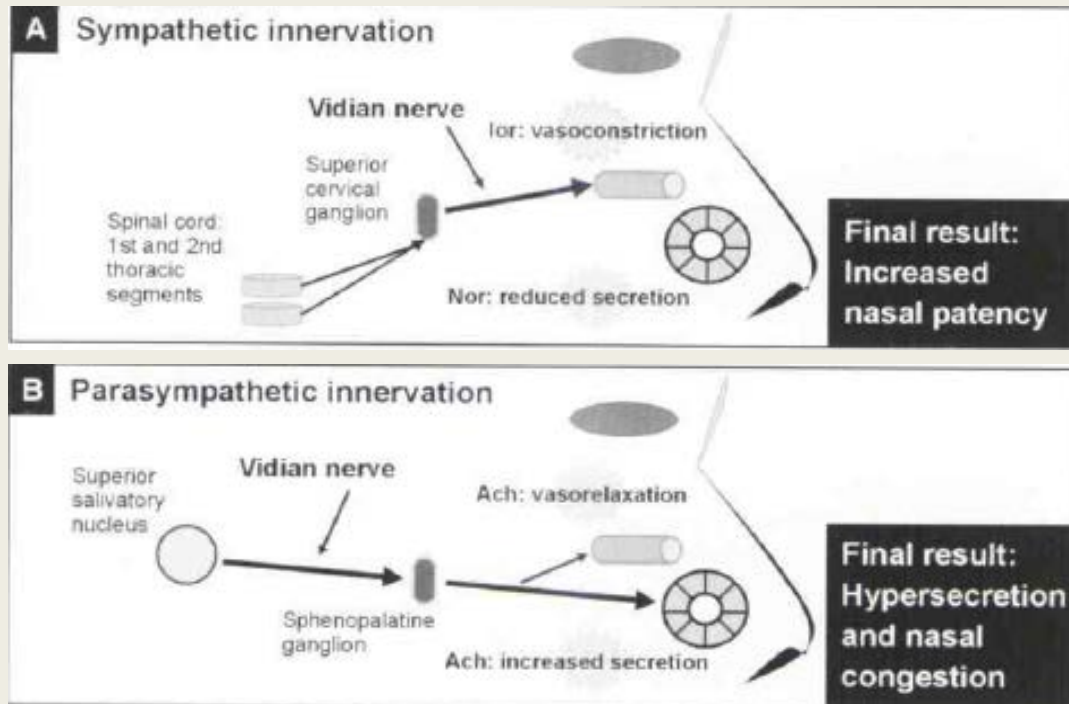
	Changes in epithelium	Edema	Dilatation of capillaries	Inflammatory cells	Hyperinnervation
Allergic rhinitis	++	+++	+++	+++	+++
Idiopathic rhinitis	—	+	++	+	+++
Control group	—	—	—	+	—

Averaged semiquantitative scores: negative —, moderate +, strong ++, very strong +++



# What if nasal steroids fail?

## 1. Imbalance of sympathetic/parasympathic nervous system



*Senile rhinitis*  
*Some forms of idiopathic rhinitis*

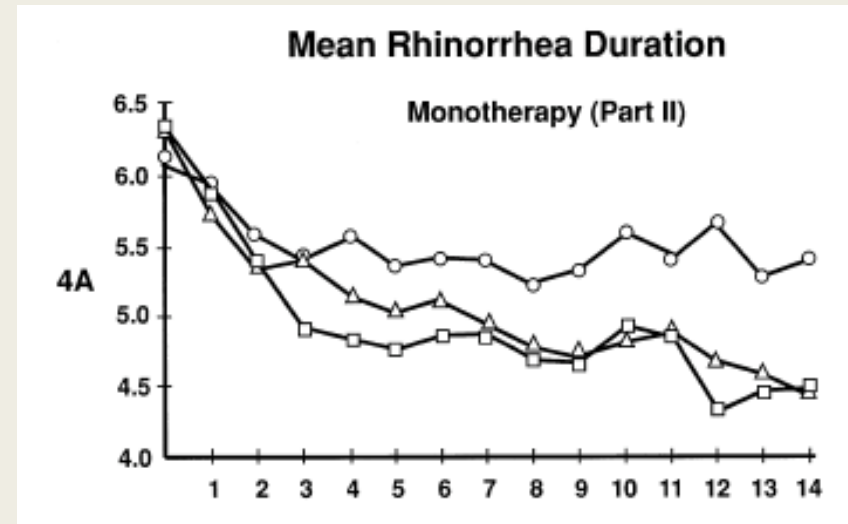
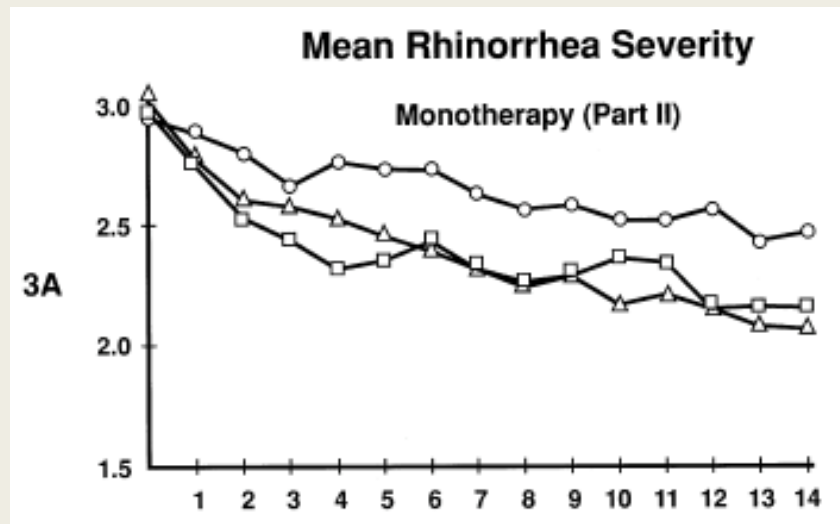
R:/ cholinergisch antagonisme



# Anticholinergic treatment

## 1. Ipratropium Bromide (Atronase)

= proven effective in treating rhinorrhea in AR and NAR



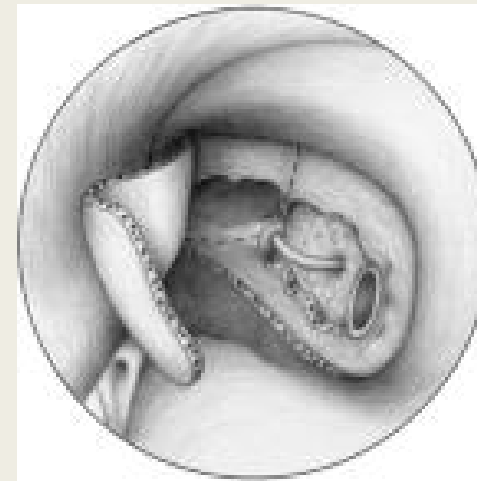
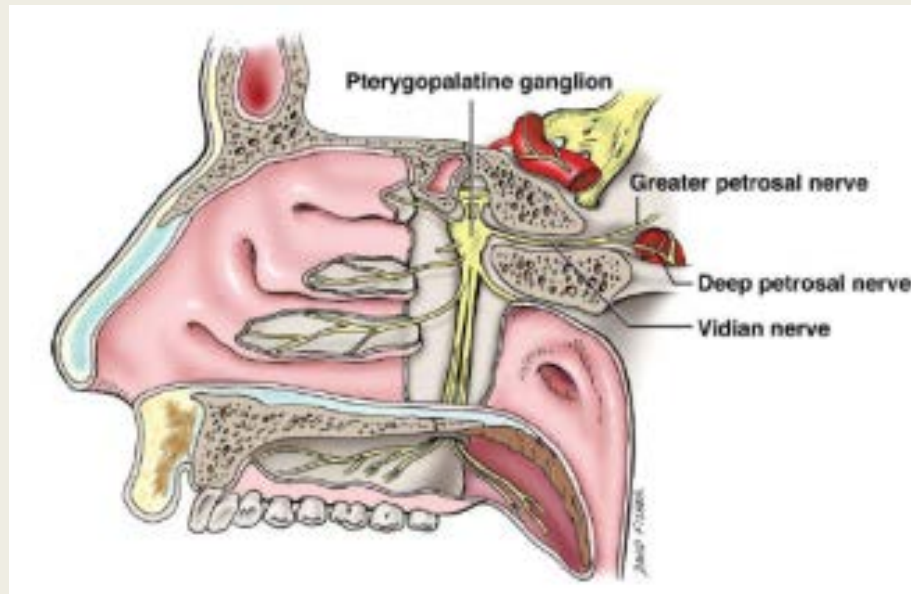
Dockhorn et al. 1999

*Treatment of choice in senile rhinitis*

*Trial in patients with mostly rhinorrhea linked to other rhinitis types*

# Anticholinergic treatment

## 2. Vidian nerve resection



Beneficial effect on most rhinitis symptoms in NAR

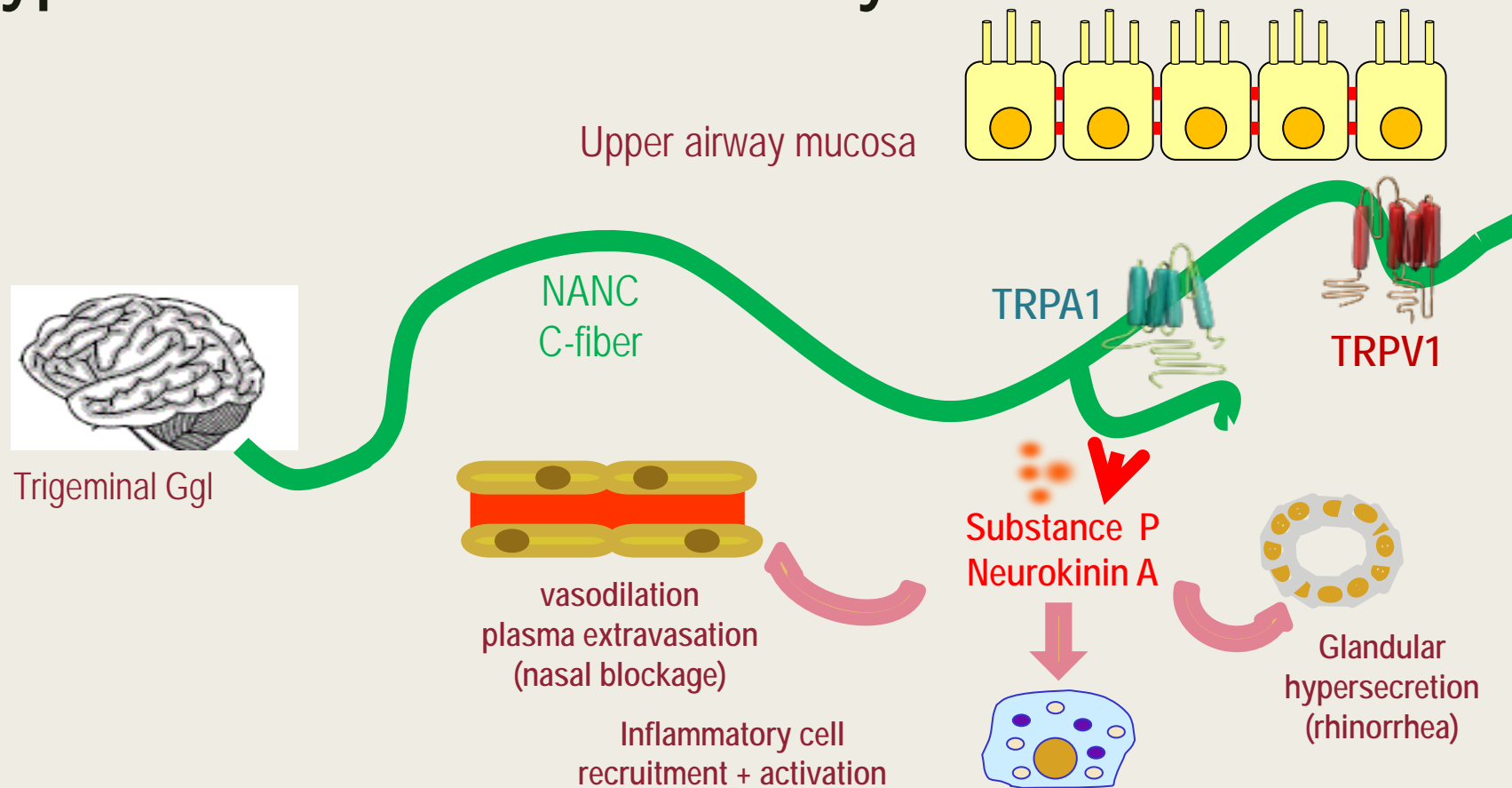
*Endoscopic approach in patients with unilateral symptoms*

*Skilled skull base surgeons !*



# What if nasal steroids fail ?

## 2. Hyperactive NANC nervous system

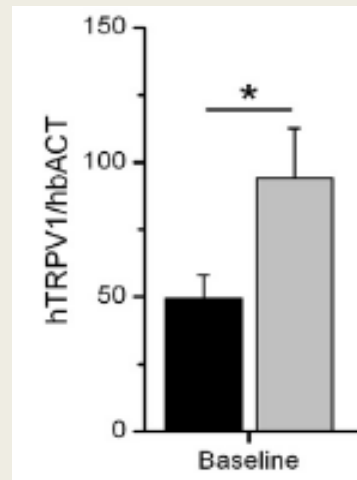
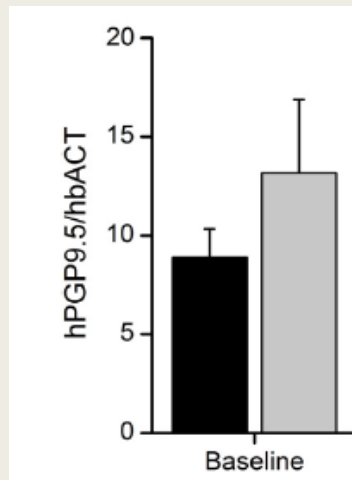




# What if nasal steroids fail ?

## 2. Hyperactive NANC nervous system

■ HC    ■ IR patients



**Crucial Role of Transient Receptor Potential Ankyrin 1 and Mast Cells in Induction of Nonallergic Airway Hyperreactivity in Mice**

*Hox et al. AJRCCM 2013*

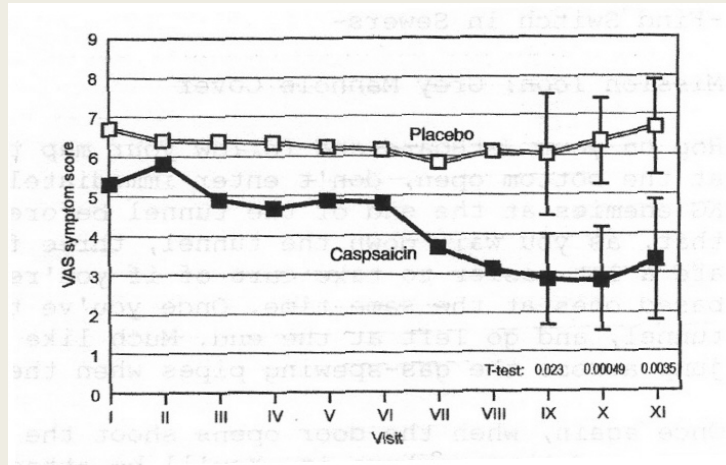
*Van Gerven et al. JACI 2014*

R:/ desensitization of the NANC nervous system



# Desensitization of the NANC system

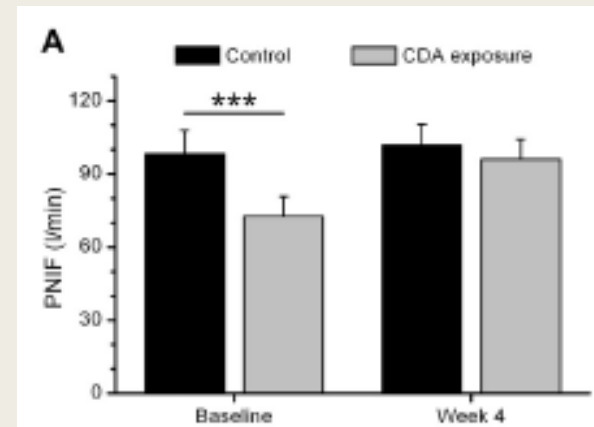
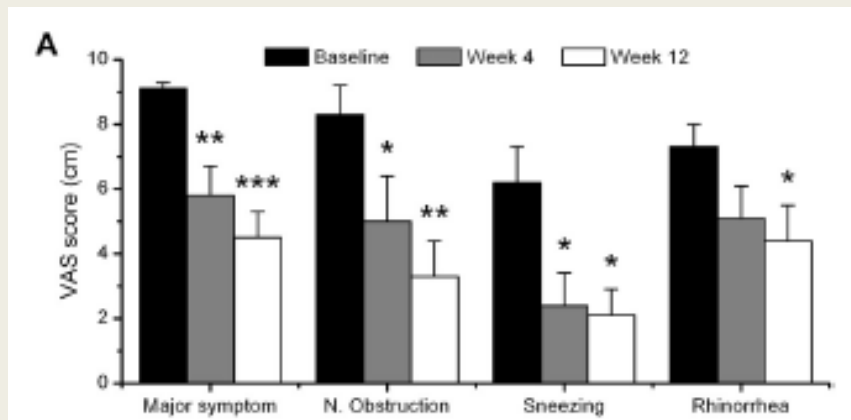
## 1. Capsaicine



Blom et al. 1997

**Low-dose capsaicin (0.01 mM) nasal spray is equally effective as the current standard treatment for idiopathic rhinitis: A randomized, double-blind, placebo-controlled trial**

Van Gerven et al. JACI 2021



Van Gerven et al. JACI 2015





# Desensitization of the NANC system

## 2. TRP channel antagonists

Inhibition of capsaicin-driven nasal hyper-reactivity by SB-705498, a TRPV1 antagonist

Carlijn Holland,<sup>1\*</sup> Cornelis van Drunen,<sup>1\*</sup> Jane Denyer,<sup>2</sup> Kevin Smart,<sup>2</sup>  
Christine Segboer,<sup>1</sup> Ingrid Terreehorst,<sup>1</sup> Amy Newlands,<sup>2</sup>  
Misba Beerahee,<sup>2</sup> Wytske Fokkens<sup>1</sup> & Daphne C. Tsitoura<sup>2</sup>

→ not commercialized, insufficient effectiveness, side-effects

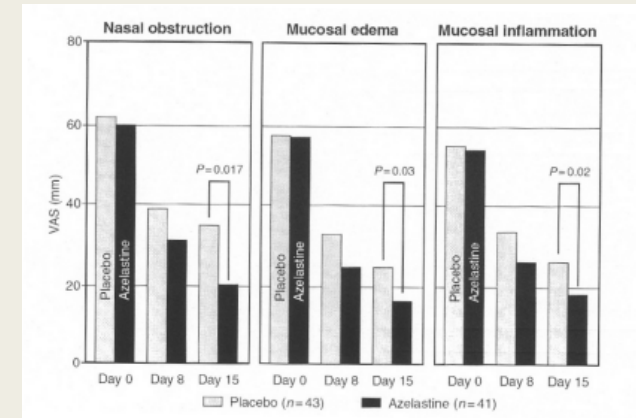
# Desensitization of the NANC system



## 3. Antihistamines: *topical azelastine*:

2 RCT have shown significant effect in NAR!

- *Anti-H1R activity*
- *Reduced Substance P release*
- *Desensitization of TRPV1* (Singh et al. Am J Rhinol 2014)



Gehanno et al. 2001

## *Nasal azelastine + Fluticasone Propionate*

- *Beneficial effect in large population of chronic rhinitis (AR+NAR) compared to fluticasone.*





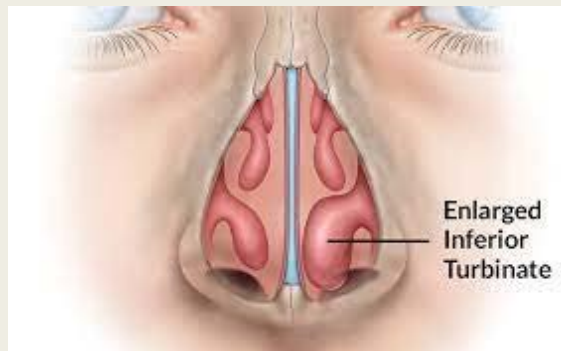
# If nothing works...

**Surgery:** Nasal obstruction patients with concomittant structural pathology

- (Rhino)Septoplasty



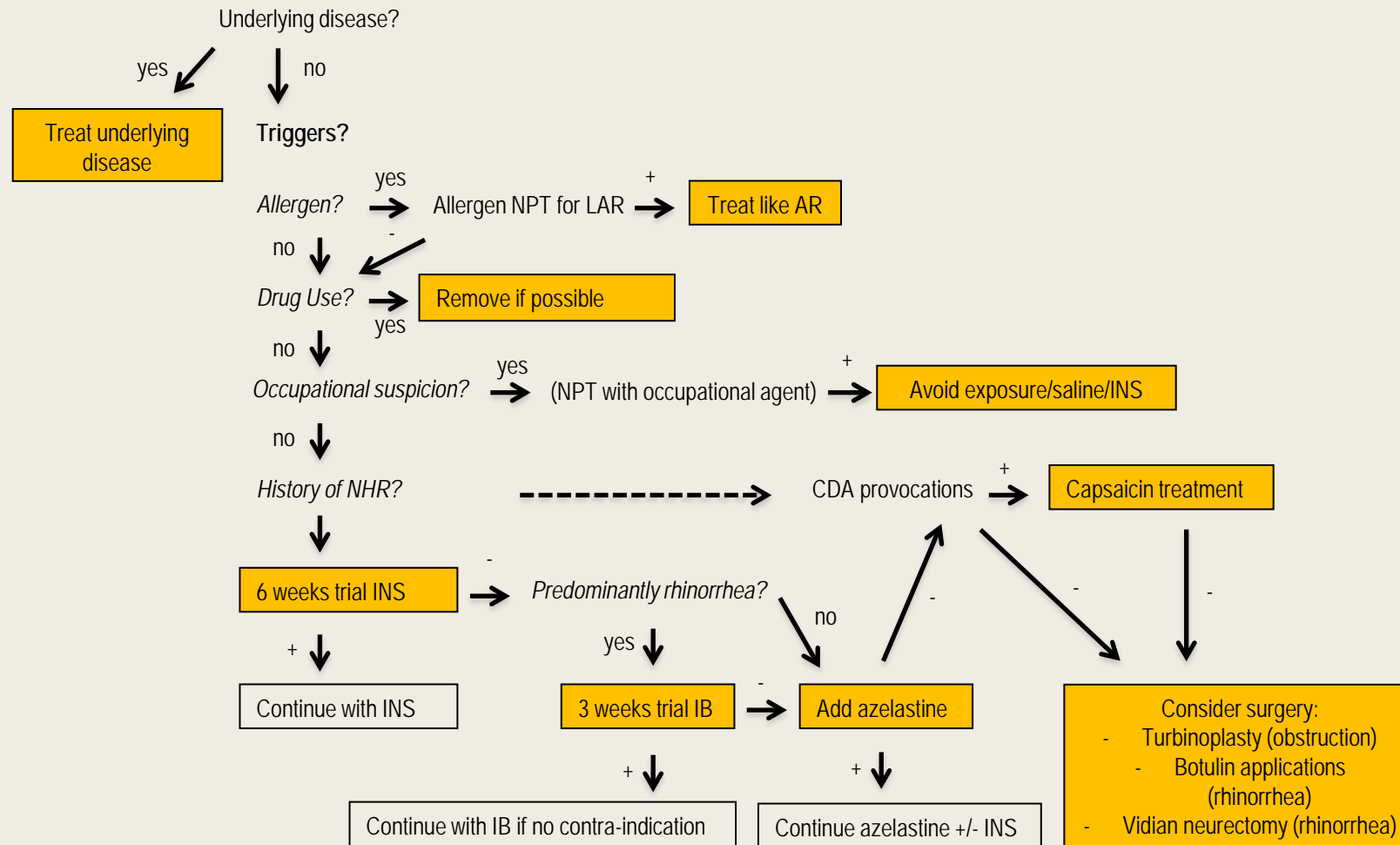
- Turbinoplasty



# Therapeutic algorithm



Chronic Rhinitis patient with negative systemic antigen-specific IgE



# Thank you !

