# Rhinosinusitis and Asthma Exacerbations


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GA²LEN
Global Allergy and Asthma European Network
Network of Excellence

# Chronic rhinosinusitis

- ***Rhinosinusitis (including nasal polyps) is defined as inflammation of the nose and the paranasal sinuses characterized by***
- **Symptoms** :nasal blockage/obstruction/congestion or nasal discharge ,facial pain/pressure, reduction or loss of smell;
- **Endoscopic findings :**polyps and/or mucopurulent discharge and/or; oedema/mucosal obstruction
- **CT changes :** mucosal changes within the ostiomeatal complex and/or sinuses.

EP3OS 2007.

# Epidemiology of CRS

- Based on symptoms 1% - 15,5%
  - „problems with sinuses”
- Increasing with age 2,7% -> 6,6%
- Gender F> M
- Geographic differences
  - 1,01% in North Korea
  - 9,9 % Scotland
- Co-morbid conditions
  - Immunodeficiency , systemic diseases
  - COPD , Bronchiectasis
  - Bronchial asthma

# Prevalence of CRS in Europe
# The GA²LEN study

- A postal questionnaire was sent to a random sample of adults aged 15-75 years in 19 centres in Europe.
- **Results** :
- the overall prevalence of CRS by EP3OS criteria was **10.9%** (range 6.9% in Germany to 27.1% in Coimbra )
- Poor corelation of CRS symtoms with objective evidence ( endoscopy/CT scanning)
- Strong, and consistent association of CRS with smoking

Tomassen P et al. Allergy 2011 ,66:556,

# Association of CRS with asthma

- CRS coexisted in 34% patients with asthma *(Annesi–Maesano 1999)*
- Abnormal sinus radiographs can be found in 53% of asthmatics *(Berman S 1974)*
- Mucosal thickening in can be visualized in 74% of patients with asthma *(Pfister R 1994)*
- Asthmatics with CRS are more likely to have NPs than nonasthmatics with CRS (57.6% versus 25%) *(Pearlman AN 2009)*

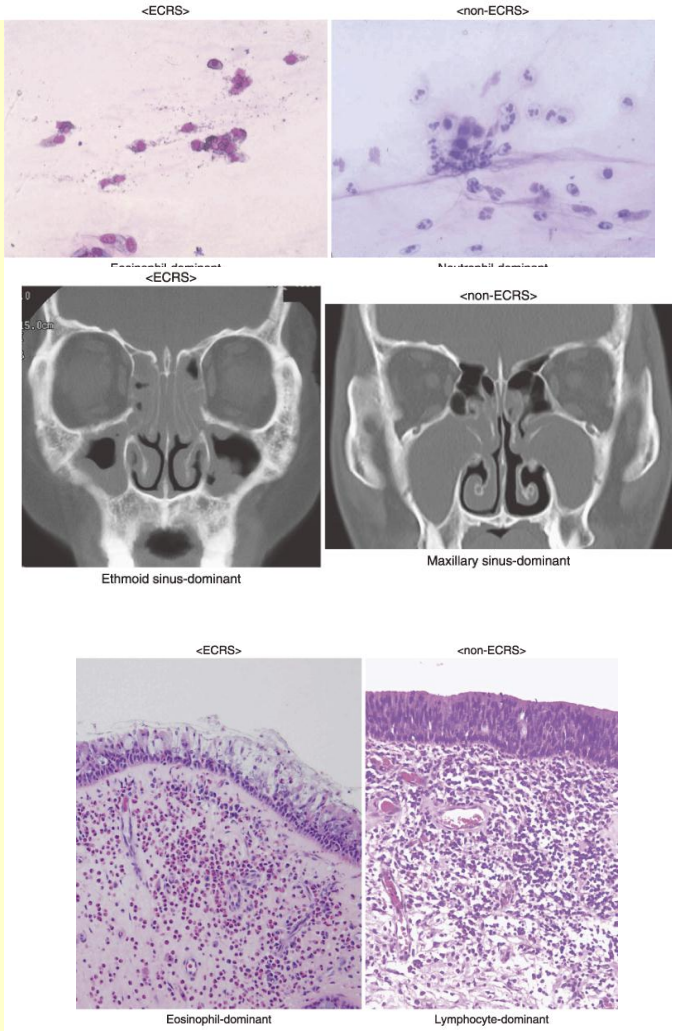
# Asthma and NP – GA2LEN Survey

- The Global Allergy and Asthma Network of Excellence (GA2LEN) conducted a postal questionnaire in representative samples of adults living in Europe to assess the presence of asthma and CRS defined by the EP3OS
- Results: Over 52 000 adults aged 18-75 years and living in 19 centres in 12 countries took part.
- There was a strong association of asthma with CRS (adjusted **OR: 3.47; 95% CI: 3.20-3.76**) at all ages.
- The association with asthma was stronger in those reporting both CRS and allergic rhinitis (adjusted **OR: 11.85;** 95% CI: 10.57-13.17).

Jarvis D et al. Allergy 2011,

# Eosinophylic versus non-eosinophylic CRS in Japan

- **Clinical features**
  - Reduction/loss of smell in early stages
  - Recurrentcy rate of nasal polyps very high
- **Endonasal findings**
  - bilateral polyps,
- **CT findings**
  - ethmoid redominance (in early stages) vs maxillary predominance (in early stages)
- **Blood examination**
  - eosinophilia
- **Therapy**
  - Macrolide therapy not effective effective
- **Coexistence of asthma**
  - more frequent

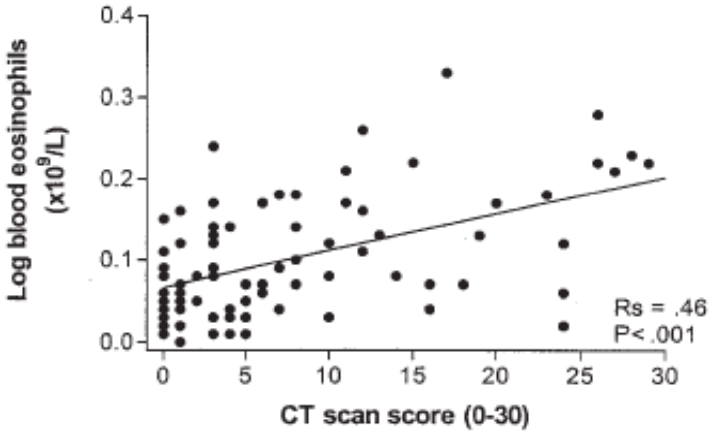



Ishitoya J et al. Allergology Int 2009.

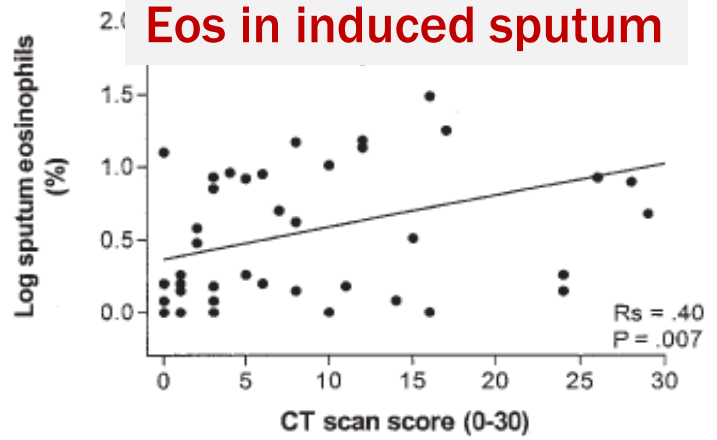
# Chronic sinusitis is related to blood and sputum eosinophilia

- In 89 outpatients with severe asthma CT scans were scored. Lung function, NO in exhaled air, and blood and sputum eosinophils were measured
- **Results**
- CT scans showed abnormalities in 84% of patients.
- There was a significant correlation between CT scores and eosinophils
  - in peripheral blood (R = 0.46)
  - In induced sputum (R = 0.40)
- level of exhaled NO (R = 0.45, P <.01)

**Eos in peripheral blood**




**Eos in induced sputum**




ten Brinke JACI 2002

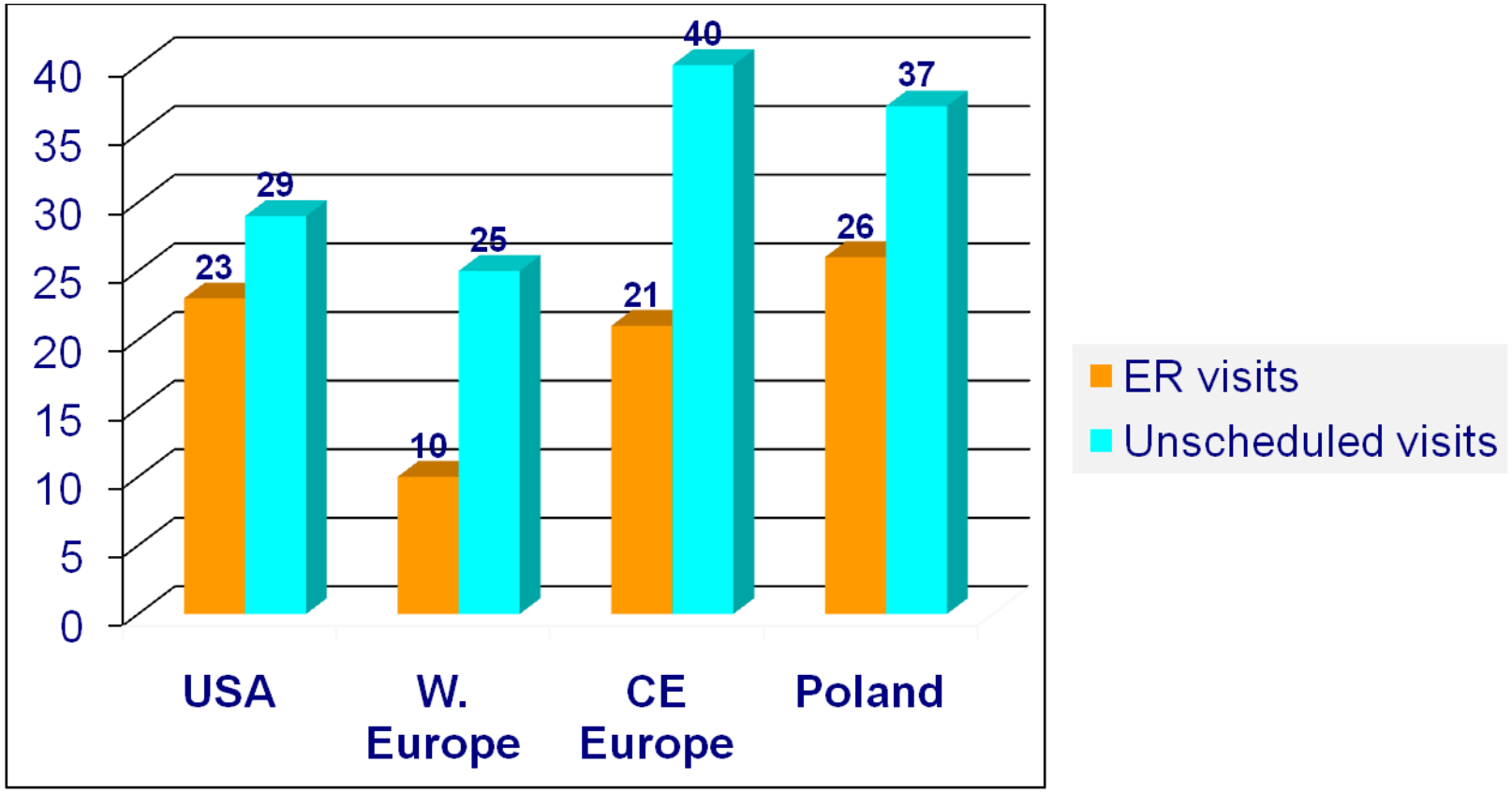
# WHO definition of asthma exacerbation

*„ Exacerbations (commonly referred to as asthma attacks or acute asthma) are episodes of progressive increase in shortness of breath, cough, wheezing, chest tightness, or a combination of these symptoms ”*

Bousquet J JACI 2010,126,926

# Asthma Inside and Reality studies

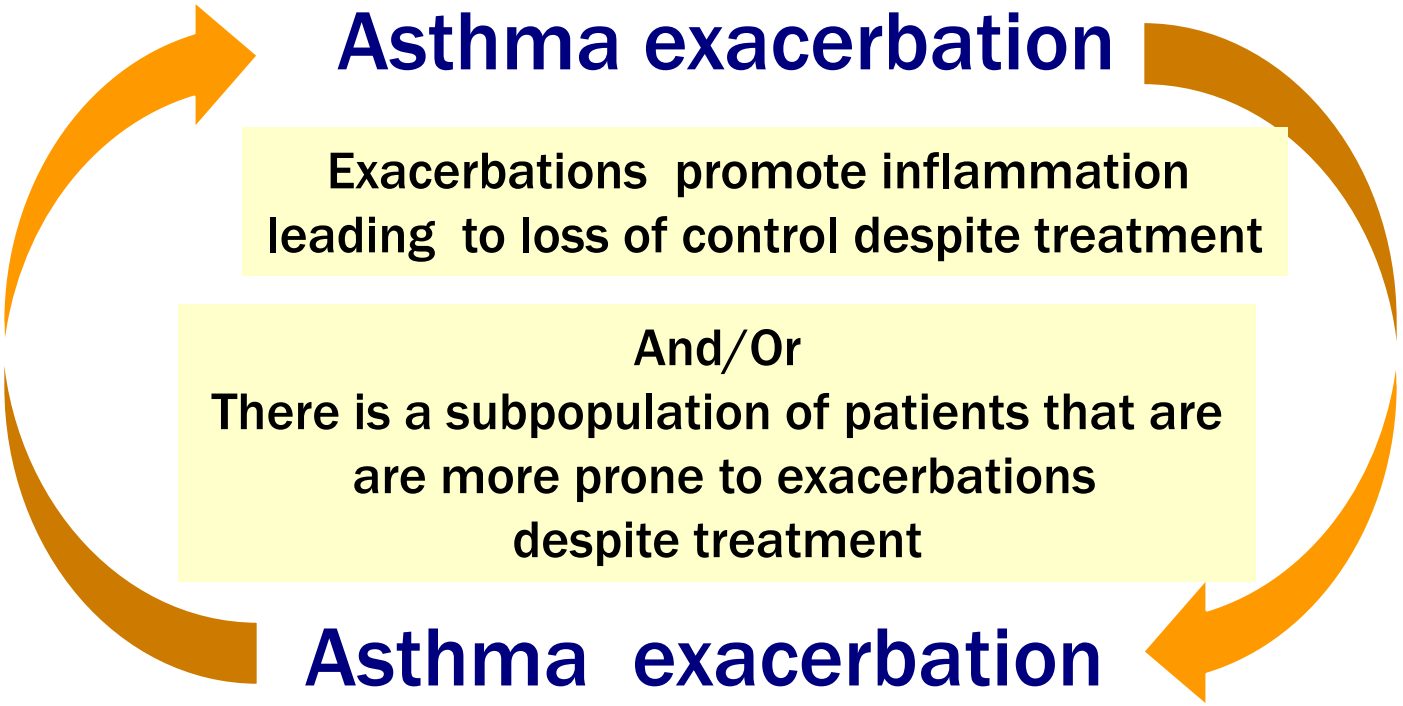
## Asthma exacerbations over last year




Rabe K. et al. : AIR study J Allergy Clin Immunol 2004

Kowalski M. L. et al.: Alergia Astma Immunologia 2004

# Consequences of asthma exacerbations




- Long term consequences of frequent asthma exacerbations
  - Accelerated loss of lung function
  - Increased risk of near fatal or fatal events

# Risk factors for asthma exacerbations

The number of ER visits is associated with:

- Older age
- Non-white race
- Lower socio-economic status
- Co-existing psychiatric diseases
- Markers of asthma severity

These factors may help to identify susceptible populations , but are not preventable

Griswold SK et al. Chest 2005

# Risk factors for frequent exacerbations

A group of 136 patients with difficult to control asthma divided in to 2 groups

- One exacerbation per year
- Three or more per year

- Risk factors for asthma exacerbations
- Psychological dysfunctioning OR=10.0
- Recurrent respiratory infections OR=6.9
- GER OR= 4.9
- **Severe CRS** **OR=3.7**
- Sleep apnea OR=3.4

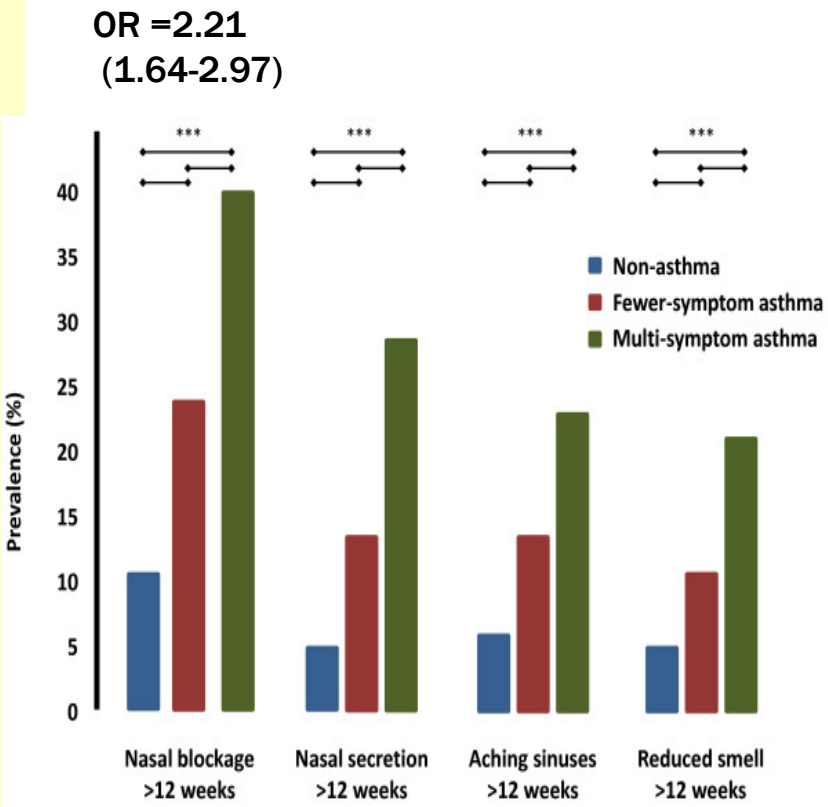
- All patients had at least one of the above factors
- 52% showed three or more factors

**Ten Brinke et al. 2005**

# More symptoms of CRS in multi-symptom asthma

- 18,087 responders in the West Sweden Asthma Study
- 2,1% ( 25% of asthmatics) had „**Multi symptom asthma**” -
- *medication and attacks of shortness of breath and recurrent wheeze and at least one out of any wheeze, dyspnoea, breathlessness-exertion, breathlessness-cold and breathlessness- exertion in cold*.

- Symptoms of CRS occurred more frequently in subjects with multi-symptom asthma compared with fewer-symptom asthma and non-asthma



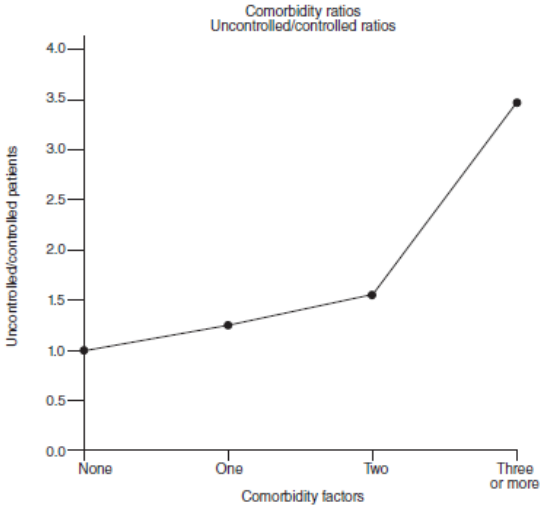

Lötvall J et al. Resp Res 2010

# Asthma comorbidity and control

- 56 controlled ( ACT>20) and 102 uncontrolled (ACT<20) asthmatics were assessed for the presence of comorbidities

**Results**

- Comorbidities more frequent in uncontrolled group
  - Nasal polyps (8.8 vs 0%)
  - Gastrooesophageal reflux (22.8 vs 8.9%)
  - ABPA (9.8 vs 0%)
- Ssimultaneous presence of 3 or more comorbidity factors was significantly more frequent in patients with sub-optimal control (*P*=.01).




Perez deLano Arch Bronchopn 2010

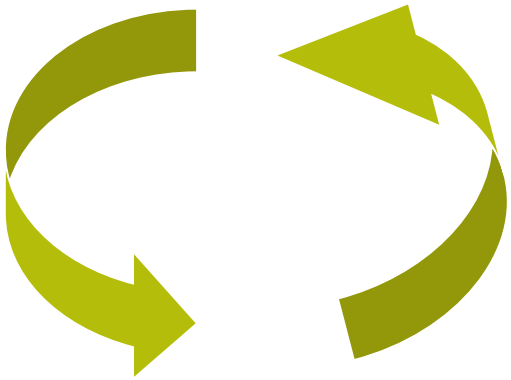
# Severe asthma (WAO definition)

**Severe asthma is defined by the level of current clinical control and risks as**

***''Uncontrolled asthma which can result in risk of***

***-frequent severe exacerbations (or death) and/or***
***-adverse reactions to medications and/or***
***- chronic morbidity (including impaired lung function or reduced lung growth in children.''***

- **asthma control**



- **asthma severity**

Bousquet J JACI 2010,126,926

# CRS/NP and asthma severity

- Presence of CRS is associated with more severe asthma *( Liou A et al. Chest 2003)*
- Presence of CRS is related to more severe asthma: higher medication use and lower FEV1

(*Aazami et al. Iran JACI 2009)*

# Relation between severity of CRS and asthma severity

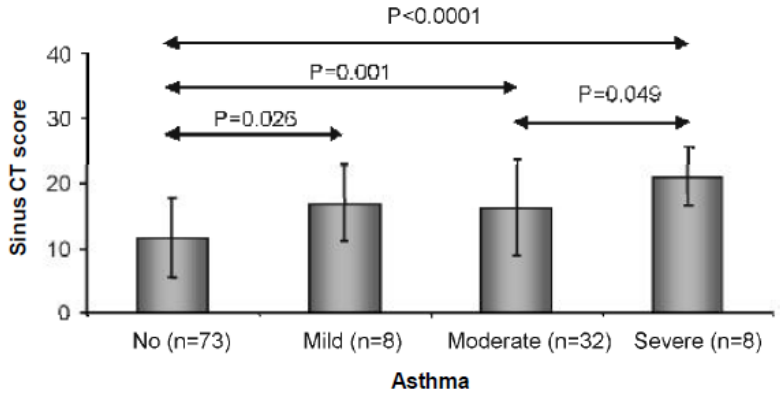
To evaluate chronic rhinosinusitis in patients with severe steroid-dependent asthma,

- **Patients and methods**
- A clinical score and coronal CT scanning were compared in 35 patients with severe corticosteroid dependent asthma and 34 mild to moderate asthmatics
- **Results**
- The proportion of patients with symptoms of rhinosinusitis was similar in both groups of asthmatic subjects (74% vs 70%)
- **All subjects** with steroid-dependent asthma **versus 88%** of subjects with mild-to-moderate asthma had abnormal CT scan results.
- The clinical and **CT scan severity scores were higher** in the subjects with severe steroid-dependent asthma.

**Bresciani M JACI 2001,107,73**

# CRS and asthma severity

- **Patients**
  A total of 121 patients with chronic rhinosinusitis ,NPs and /or asthma were evaluated (sinus CT scans and nasal endoscopy )
- **Results**
- Patients with CRS/NP/asthma ( as compared to CRS only ) had: more severe sinus disease on CT scan (P<0.001), greater bronchial obstruction (P<0.05),
- The extent of sinus CT changes was greater in asthmatics and correlated with greater duration of asthma (P<0.0001), and age (P=0.039




Staikūniene J Medicina 2008,44,257

# Mechanisms linking CRS/NP. with asthma

CRS and asthma share common:

- Histopathology
- Immunopathology
- Patomechanism ?

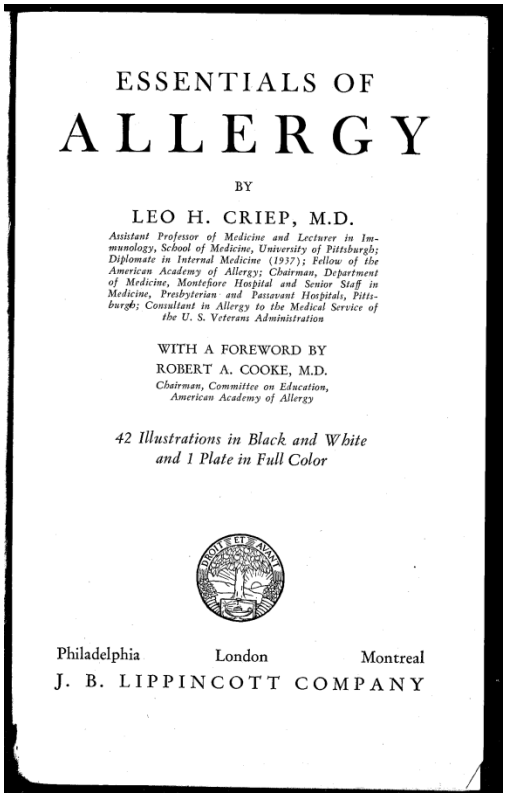
- Aspiration
- Mouth breathing
- Neurogenic reflex
- Common triggers
  - Infectious agents
  - Allergens
  - Other environmental ( e.g. tabacco smoke)
- One airway disease – involvement of bone marrow

Chapter: Treatment of asthma:

Removal of infection and nasal surgery

*‚In view of the fact, that so many patients who have bronchial asthma have an associated paranasal sinus infection, proper and adequate management of such infections becomes very important'*

*‚Asthmatic patients may show temporary improvement following surgery … however ‚such operations usually do not lead to permanent relief ..'*



ESSENTIALS OF

ALLERGY

BY

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WITH A FOREWORD BY

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*42 Illustrations in Black and White and 1 Plate in Full Color*

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**1945**

# Effect of CRS treatment on bronchial asthma

## Medical treatment

- Improvement in asthma symptoms
- Decrease in using bronchodilators
- Improvement in spirometry
- Improvement in severity of asthma

| | |
|---|---|
| *Slavin RG* | *1982* |
| *Rachalevsky GS* | *1984* |
| *Friedman R* | *1994* |
| *Tosca* | *2003* |
| *Lamblin C et al.* | *2000* |

## Surgical treatment

- Improvement in symptoms
- Decrease in asthma medication ( including OCS)
- Improved pulmonary function
- Decrease in BHR

| | |
|---|---|
| Ikeda K | 1999 |
| Palmer JN | 2001 |
| Okayama M | 1998 |
| Enhage A | 2009 |

# Effect of medical versus surgical CRS/NP therapy on asthma (2)

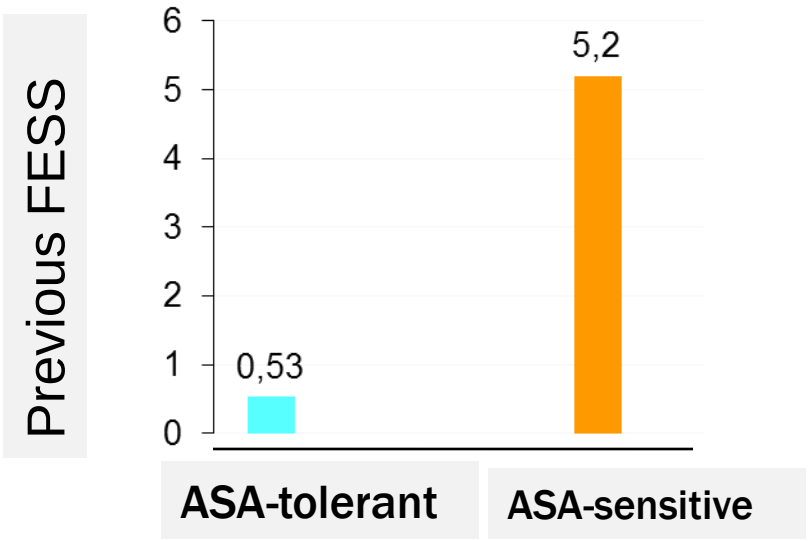
Effect on asthma exacerbations:

- Surgery reduced the number of hospitalizations for asthma **from seven** ( in three preoperative 12 months) **to two (**post-operatively) ($p<0.05$)
- The medical treatment of CRS reduced hospital admissions from **five to one** ( $p<0.05$)
- No difference between surgical and medical treatment

Ragab s et al. ERJ 2006,28,68

# Severity of CRS and asthma in patients with AERD

**Recurrence of nasal polyps after FESS**




- **Patients with AERD had history of 10 times as many previous FESS procedures as had the patients without aspirin sensitivty**

**Higher asthma severity in AERD**

- Higher medication requirements, including dependence on oral GCS *(Szczeklik A. et al. 2000)*
- More likely to have been intubated and to have a steroid burst in the previous three months *( **Mascia K et al . 2005**)*
- Frequent exacerbations *( Koga T. Et al. 2006)*
- Association with near fatal asthma *( Plaza W. et al. 2002)*

***Kim JE Ear Nose Throat J. 2007 Jul;86(7):396-9.***

# Endoscopic Sinus Surgery and asthma outcomes in AIA and ATA

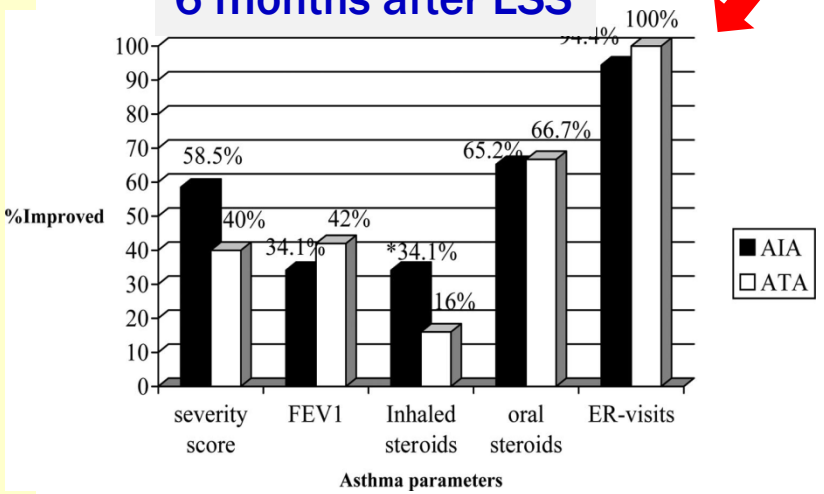
## Patients

- 91 patients with CRS resistant to medical treatment
  - 50 ASA-tolerant
  - 41 ASA- sensitive
- Patients were subjected to ESS and followed at 6 and 12 months after surgery

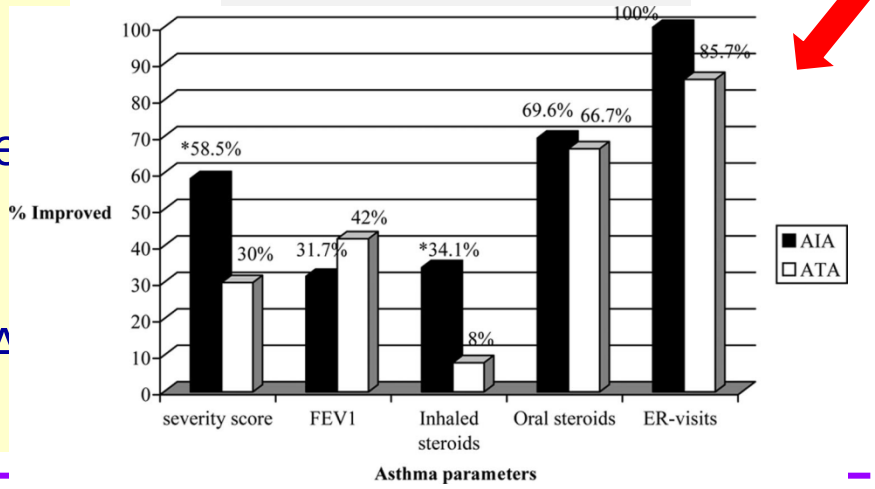
## Results

- Improvement in asthma outcome
  - FEV1, ICS, OCS
  - Exacerbations
- Similar response in AIA and ATA

**6 months after ESS**




**12 months after ESS**



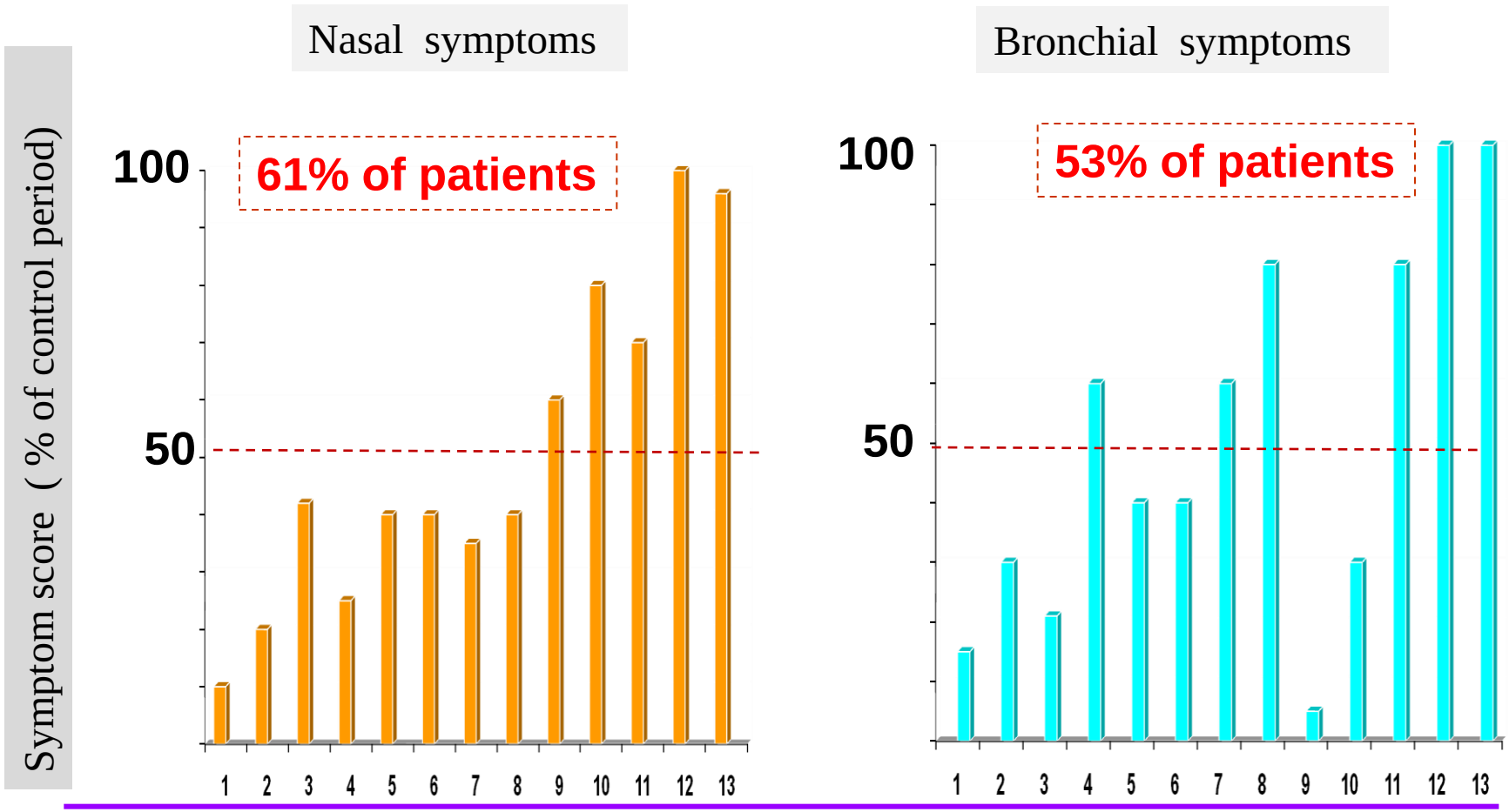

). G Awad et al. (Am J Rhinol 22, 197–203, 2008;)

# Aspirin desensitization in patients with AERD

- 1923 F. Vidal reported „desensitization” to aspirin
- 1976 C. R. Zeiss & R.F. Lockey described refractory period to aspirin
- 1981 D.D. Stevenson reported clinical benefits of prolonged treatment with aspirin after desensitization

- Daily oral ASA after desensitization (300- 2400mg) in some patients may lead to:
  - **Improvement in asthma symptoms**
  - **Improvement in rhinosinusitis symptoms**
  - **Decreased need for sinus surgery/polypectomy**

# Rapid effect of treatment with 600 mg/day of ASA on nasal and bronchial symptoms in ASA-sensitive asthmatics

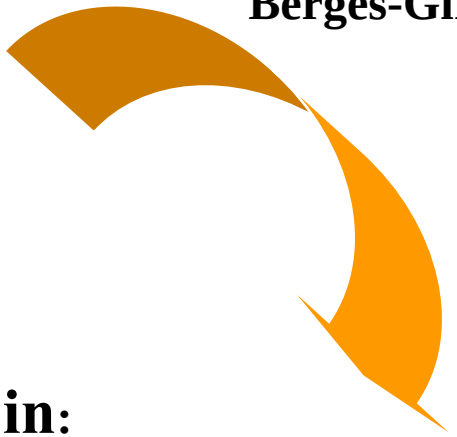



*Kowalski ML et al. Eur. Resp J. 1986, 69,219-25*

# Long–term treatment with aspirin after desensitization

**172 patients desensitized**
**126 patients followed up for a year**
**650 mg ASA bid at home**
**Clinical assessment: 6 month and 1 year**

**Berges-Gimeno JACI 2003,111,180-6**



**In 87 % of patients decrease in:**

- Number of sinus infections and surgical procedures
- Symptom score ( sens of smell)
- Medications use

- Global assessement of asthma activity
- Hospital admissions and ER visits
-

# Conclusions

- Presence of CRS in a patient with asthma may increase asthma severity and decrease asthma control, leading to increased asthma excerbations.
- Proper management of CRS may improve asthma control and reduce the risk of asthma exacerbation.

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