ACCURATE DIAGNOSIS OF ALLERGIC AIRWAY DISEASES

Prof Dr Philippe GEVAERT
DISCLOSURES

Phillipe Gevaert, MD, PhD, has disclosed the following relationships: Served as an advisor or speaker and received grant/research support from: 3NT, Ablynx, ALK, Argenx, Bekaert Textiles, Genentech, GSK, Hall Allergy, Medtronic, Novartis, Regeneron, Roche, Sanofi-Genzyme, Teva, and Thermo Fisher
ACCURATE DIAGNOSIS OF ALLERGIC AIRWAY DISEASES

History
Inspection
Clinical Examination

Sensitisation
Nasal patency
Nasal provocatio

Precision medicine
SYMPTOMS OF ALLERGIC RHINITIS

4 MAJOR NASAL SYMPTOMS

sneezing
itchy nose
rhinorrhoea

nasal obstruction

NOTE
most important symptom!
Clinical assessment of rhinitis

- History
  - Nasal discharge
  - Blockage
  - Sneezing/itch

- 2 or more symptoms for >1 hr on most days

- "Sneezers and runners"
  - Sneezing
  - Rhinorrhea
  - Itching
  - Nasal blockage
  - Diurnal rhythm
  - Conjunctivitis
  - Especially paroxysmal watery anterior and posterior
  - Yes
  - Variable
  - Worse during day improving at night
  - Often present

- "Blockers"
  - Little or none
  - Thick mucus more posterior
  - No
  - Often severe
  - Constant, day and night, may be worse at night
**HISTORY TAKING IN ALLERGIC RHINITIS**

**Seasonality** of symptoms

### Pollen Calendar

<table>
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<tr>
<th>Pollen Type</th>
<th>Feb</th>
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HISTORY TAKING IN ALLERGIC RHINITIS

**seasonality** of symptoms

**influencing factors**
aggravating vs alleviating factors

Cave: Nasal Cycle!
HISTORY TAKING IN ALLERGIC RHINITIS

**seasonality** of symptoms

**influencing factors**
aggravating vs alleviating factors

**duration** of symptoms

<table>
<thead>
<tr>
<th>Intermittent</th>
<th>Persistent</th>
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<td>. &lt; 4 days per week</td>
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<td>. or &lt; 4 weeks</td>
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Persistent
= ≥ 4 days per week
= ≥ 4 weeks
HISTORY TAKING IN ALLERGIC RHINITIS

seasonality of symptoms

influencing factors
aggravating vs alleviating factors

duration of symptoms

effects on general well-being
Quality of life
<table>
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<th>ARIA CLASSIFICATION</th>
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<td>- &amp; normal work and school</td>
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<td>- &amp; no troublesome symptoms</td>
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in untreated patients
CLASSIFICATION OF AR PATIENTS IN GENERAL PRACTICE DURING POLLEN SEASON

N=804 subjects with GP-based diagnosis

Van Hoecke et al, 2005
ARIA classification

SEVERITY

MILD
0-5 cm (7%)

MODERATE / SEVERE
6-10 cm (93%)

% patients

0  2.5  5.0  7.5  10.0  12.5  15.0

VAS ( cm )

0  1  2  3  4  5  6  7  8  9  10

Mild  < 5
Mod/Severe  > 6

HISTORY TAKING IN ALLERGIC RHINITIS

Family history of allergy: Eczema

Food allergy: Oral allergy syndrome (birch – apple)

Asthma: cough - dyspnea

Occupation: exposure to allergens / irritants relation to symptoms

Medication use: reactions to medication e.g. aspirin use of decongestant sprays
INSPECTION OF THE NOSE

SIGNS OF ALLERGIC RHINITIS in children

- Open mouth breathing: adenoids?
ANTERIOR RHINOSCOPY & NASAL ENDOSCOPY
SEPTAL PATHOLOGY
ACCURATE DIAGNOSIS OF ALLERGIC AIRWAY DISEASES

History
Inspection
Clinical Examination

Sensitisation
Nasal patency
Nasal provocation

Precision medicine
Skin prick tests

+ AR symptoms

N=2320

40% SENSITISATION
29.8% SPT+ AR SYMPTOMS

Blomme K Int Arch Allergy Immunol 2013;160:200–207
Regional variation in the prevalence of sensitization to common aeroallergens in adults: the GA²LEN survey


Table 2: Population prevalence (95% CI) of sensitization to each allergen and population geometric mean total immunoglobulin E (IgE) (95% CI) in each zone

<table>
<thead>
<tr>
<th>Subpopulation</th>
<th>Dermatophagoides pteronyssinus (%)</th>
<th>Dermatophagoides farinae (%)</th>
<th>Bird (%)</th>
<th>Artemisia (%)</th>
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Region specific extracts
RAST – MOLECULAR ALLERGOLOGY - MULTIPLEX

RAST

classical ImmunoCAP assay

Single-analyte assay: single analysis of specific IgE directed against single allergens, single allergen components or mixtures of allergens

ISAC (Immuno Solid-phase Allergy Chip)

ImmunoCAP ISAC (16 spots per mm²)

Multiplex assay: multiple analysis of specific IgE directed against allergen components in one single run
NASAL PATENCY AND AIRFLOW

- Mirror test
NASAL PATENCY AND AIRFLOW

- Mirror test
- Rhinomanometry
NASAL PATENCY AND AIRFLOW

- Mirror test
- Rhinomanometry
- Acoustic rhinometry
NASAL PATENCY AND AIRFLOW

- Mirror test
- Rhinomanometry
- Acoustic rhinometry
- Nasal inspiratory / expiratory peak flow
Short-Time Cold Dry Air Exposure: A Useful Diagnostic Tool for Nasal Hyperresponsiveness

Laura Van Gerven, MD; Guy Boeckxstaens, MD, PhD; Mark Jorissen, MD, PhD; Wytske Fokkens, MD, PhD; Peter W. Hellings, MD, PhD
NASAL NITRIC OXIDE
(G SCADDING, CURR OPIN OTOLARYNGOL HEAD NECK SURG. 2007)

- main source = paranasal sinuses
- 100-fold higher relative to lower airways
- Useful in PCD

Figure 1 The very different levels of nitric oxide in sinuses, upper and lower airways

NO in respiratory tract

- Continuous production in sinuses
- Inducible in airways

20–25 ppm
400–900 ppb
<20 ppb

NO levels in nasal disease

High
900
Inflammation

“Normal”
400

Low
100
Blockage/polyps/CF

Very low
PCD
### Unmet needs in the Methodology

- Allergen **dose** and quality
- Allergen **application** technique
- The need of a **titration** process
- Provocation of either **one** or **two nostrils**
- The method to **assess** subjective and objective **outcome**

Augé, *Allergy* 2018
ALLERGEN CHALLENGE: INDICATIONS FOR THE CLINICAL PRACTICE

**Diagnosis of Allergic Rhinitis**

- To evaluate the *clinical significance* of individual allergens in *multisensitized* patients
- To solve *discrepancies* between the *clinical history* and the *IgE-sensitization* tests

**Design composition of allergen immunotherapy**

- Local Allergic rhinitis
- Occupational rhinitis
- Evaluate *ocular* symptoms

**Evaluation of the effect of allergen immunotherapy** in allergic rhinitis

- To follow up and monitor the clinical response to allergen immunotherapy
APPLICATION TECHNIQUE FOR SPRAY DEVICES

**Bilateral application by spray vial with a 50 μl nozzle**

- **Test puff** prior to the challenge
- **Two puffs of 50 μl/each per nostril**

**Patient’s collaboration**
- Breath deeply before
- Hold breath during
- Exhale profoundly after

To prevent aerosol penetration of the lower airways

Avoid to spray towards the nasal septum

EAACI PP 2018
SUMMARY OF METHODOLOGICAL RECOMMENDATIONS

To use **standardized** allergen solutions

To perform the Nasal Allergen Challenge **bilaterally**

To **spray** 2 puffs (0.1 ml/nostril)

**Micropipette** (100μl/nostril)

Visual Analogue Scale (VAS)

**Anterior Active Rhinomanometry**

**Acoustic Rhinometry**

Augé, *Allergy* 2018

ACCURATE DIAGNOSIS OF ALLERGIC AIRWAY DISEASES

History
Inspection
Clinical Examination

Sensitisation
Nasal patency
Nasal provocation

Precision medicine
WE HAD A DREAM (AND STILL HAVE A DREAM)

Diagnosis

Sample

Personalized treatment

GHENT UNIVERSITY
RELIABLE MITE-SPECIFIC IGE TESTING IN NASAL SECRETIONS BY MEANS OF ALLERGEN MICROARRAY.

Berings M1, Arasi S2, De Ruyck N3, Perna S4, Resch Y5, Lupinek C5, Chen KW5, Vrtala S6, Pajno GB7, Bachert C3, Lambrecht BN8, Dullaers M9, Valenta R5, Matricardi PM4, Gevaert P3.

---

**A**

Filter Disks
10 mm diameters
Cellulose and cotton fibres

Ear Packs
2.4 cm x 1.2 cm diameters
PVA sponge material

Sinus Packs
3.5 x 0.9 x 1.2 cm
PVA sponge material

---

**B**

---

**C**

![Graphs showing correlation between nasal IgE levels and serum IgE levels](Graphs.png)

- Filter Disks: $r_s = 0.43$, $p < 0.001$
- Sinus Packs: $r_s = 0.45$, $p < 0.001$
- Sinus Packs: $r_s = 0.78$, $p < 0.001$
RELIABLE MITE-SPECIFIC IGE TESTING IN NASAL SECRETIONS BY MEANS OF ALLERGEN MICROARRAY.

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ImmunoCap ISAC
- Genomics: all the genes
  - pharmacogenomics: choice of personalized medicine
  - nutrigenomics: choice of best diet
  - toxicogenomics: prediction of toxicity
- Epigenomics: all epigenetic changes in genome
- Transcriptomics: all the mRNAs → microarrays
- Proteomics: all the proteins
- Interactomics: all interactions between all proteins
- Metabolomics (or metabonomics): all metabolites
- ...
CURRENT TECHNOLOGICAL REVOLUTION …
POSITIONING THE PRINCIPLES OF PRECISION MEDICINE IN CARE PATHWAYS FOR ALLERGIC RHINITIS AND CHRONIC RHINOSINUSITIS


GRADED IMPLEMENTATION of PRECISION MEDICINE

 Prediction of success
 Participation

 Prediction of success
 Prevention strategy
 Participation

 Prediction of success
 Personalized care
 Prevention strategy
 Participation
PRECISION MEDICINE PRINCIPLES
ALLERGIC RHINITIS

**PRIMARY LEVEL**
- Prediction of success
- Participation

**SECONDARY LEVEL**
- Prediction of success
- Prevention strategy
- Participation

**TERTIARY LEVEL**
- Personalized care
- Prediction of success
- Prevention strategy
- Participation

- Effects of different treatment options on nasal, ocular, bronchial symptoms and QoL
  - Oral vs nasal treatment
  - Mono vs combined treatment
  - Steroidal vs non-steroidal treatment
  - Pharmacotherapy vs AIT

- Step-up or step-down treatment
  - SECONDARY prevention: pharmacotherapy, AIT and control of environmental triggers
  - TERTIARY prevention: prevention of organ damage

- ENDOTYPE-driven treatment plan

- Design of patient-centered treatment plan, taking into account patients' preference and availability/affordability of treatment
  - AIT vs biological treatment
ACCURATE DIAGNOSIS OF ALLERGIC AIRWAY DISEASES

- History
- Inspection
- Clinical Examination
- Sensitisation
- Nasal patency
- Nasal provocation
- Precision medicine