Diagnostic tools in Rhinology

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• Introduction

There are several reasons for accurate investigation of upper airways disorders like allergic rhinitis and rhinosinusitis.
1/ The first reason relates that such problems impact very significantly upon patients' quality of life and that well directed treatment can decrease the impairment of quality of life.
• 2/The second is that some of these disorders are severe with significant morbidity and even mortality, and that presentation often occurs in the upper airway. Early diagnosis and effective management can prevent serious consequences, like in Wegener's granulomatosis.
3. The third reason relates to the fact that upper respiratory tract problems exacerbate lower respiratory symptoms and may extend to involve the lower respiratory tract.

Because the nose is an air conditioner; filtering, warming and humidifying over 10,000 liters of air daily before it progresses to the lungs.
Diagnostic tools are:
History of the Patient

• The patients' history is vital in understanding and diagnosing the problem.

• In rhinitis and rhinosinusitis an accurate history is usually more important than any other investigation.
Example

1. Allergic Rhinitis
   Typical symptoms of AR include rhinorrhea, sneezing, nasal obstruction and pruritus
   • eye symptoms: redness, discharge, itching, and vision impairment.
   • Symptoms related to reduced smell and taste are more typical of rhinosinusitis.
   • timing of symptoms (intermittent vs persistent disease, )
   • severity of symptoms (mild, moderate or severe)
   • provoking factors e.g. animal contact
     • occupational aggravation e.g. animal care facility
     • seasonal aggravation e.g. grass pollen season
   • effects of treatments tried in the past
   • intolerance to medication e.g. aspirin
   • associated oral allergy symptoms

Allergy is a more likely diagnosis if there is a past, present or family history of allergic diseases (AR, asthma, atopic dermatitis).
• Nasal Examination
I. GENERAL INSPECTION

• Inspection is the visual investigation of the external structures of the nose and beyond, in order to get a first and superficial impression of the nose and nasal function.

• Major anomalies can be visualized directly, like nasal vestibulum stenosis in cleft lip patients

• collapse of the nostrils during inspiration or severe septal deviations
II. Palpation

To evaluate the nose with the fingertips, to search for shape or tissue anomalies, painful or sensitive areas,
• and/or lack of tip support mechanisms.
Anterior Rhinoscopy

Internal inspection of the vestibulum and cavum nasi with the aid of an examination lamp fixed to a headband and a nose speculum.

Can see Possible clinical findings:

- Rhinorrhae with transparent or discolored secretions,
- Asymmetries (mostly of the nasal septum),
- Mucosal edema,
- Nasal polyps, neoplasm's,
- Can assess the accessibility of the nose and the shape of the conchae.
• Sensitivity
Anterior rhinoscopy is limited in its evaluation of the entire nasal cavity.

• Therefore, complete and thorough examination using nasal endoscopy is recommended for patients with nasal symptoms. For example, small polyps may not be seen by anterior rhinoscopy.
Posterior Rhinoscopy

- An inspection of the posterior parts of the cavum nasi and the nasopharynx with the aid of a small throat mirror

Possible conditions are seen like congenital choanal atresia, acute adenoiditis, irritation of the rhinopharynx, post-nasal discharge, antro-choanal polyps

- At present, this examination is not routinely being performed, and is often replaced by nasal endoscopy
Nasal Endoscopy (rigid and flexible)

- endoscopy, a good evaluation of the septum, the whole nasal cavity and the nasopharynx is possible, but also the area of the middle meatus which has clinical importance in rhinosinusitis.

Rigid endoscopy has proven to be more patient friendly

- supplies a better image than flexible endoscopy

- The pain scores were similarly in favor of the rigid scope, showing less discomfort
Diaphanoscopy of the maxillary sinus

• Transillumination of the maxillary sinus is performed with a light source in the mouth of the patient, watched in a darkened room. If the sinus is accessible the light shines through the sinus and through the pupil.

• diaphanoscopy method was widely used for about half a century

But in the end could not compete with modern techniques of radiography and ultrasound
Allergy Tests Including Provocation

• diagnostic process of allergic rhinitis we assume that allergen-specific IgE is the triggering factor of symptoms and of the underlying inflammatory process.

-Thus, the main goal of the diagnostic tests is to demonstrate both the presence and functional relevance of such IgE.
- the presence of specific IgE alone (sensitization) does not necessarily imply the existence of allergic symptoms, and there are a relevant number of individuals who are sensitized but who are not clinically allergic

- The presence of specific IgE can be demonstrated either in vivo (skin tests, SPT) or in vitro by detecting allergen-specific IgE in the blood (RAST, CAP-RAST and equivalent assays)
• Skin prick test (SPT)
• The SPT technique is currently considered the gold standard method for the diagnosis of allergic rhinitis.

• With a trained investigator, they are highly reproducible

• always must include a negative (saline or diluent) and a positive control (histamine HCl 0.1%).

Skin tests should be read at the peak of reaction (approximately at 15 minutes) by measuring the extension of wheals

• late reactions is not known
the interpretation of a positive test must be integrated with the clinical history, since a positive SPT does not always imply a clinically relevant sensitization.

False positive reactions may occur, if a dermographism is present, but this can be ruled out with the use of the negative control.

False negative may occur due to:

a) weak potency of the extract;

b) inadequate technique (weak puncture);

c) interfering drugs.
Systemic antihistamines are the most important drugs that reduce the skin reaction. Thus, antihistamines must be discontinued at least 5 days before the SPT.

On the other hand, antileukotrienes do not interfere with SPT and can be continued.
### Drugs affecting the results of skin tests

#### Suppression

**Duration of Suppression (days)**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Duration of Suppression (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cetirizine, desloratadine, ebastine, levocetirizine, mizolastine</td>
<td>++++ 3-10</td>
</tr>
<tr>
<td>Chlorphenamine, promethazine</td>
<td>++ 1-3</td>
</tr>
<tr>
<td>Ketotifen</td>
<td>++++ &gt;5</td>
</tr>
<tr>
<td>Imipramine</td>
<td>++++ &gt;10</td>
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<tr>
<td>Inhaled steroids</td>
<td>-</td>
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<tr>
<td>Systemic steroids</td>
<td>+/-</td>
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<tr>
<td>Cimetidine/ranitidine</td>
<td>-</td>
</tr>
<tr>
<td>Antileukotrienes</td>
<td>-</td>
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</tbody>
</table>
• Intradermal tests are not of choice for the diagnosis of respiratory allergy, since they do not perform better than SPT and can induce false positive results.

- Atopy patch tests: patients with atopic dermatitis show only atopy patch test positivity while specific IgE to the same allergen remains negative but the atopy patch test is usually not relevant for the diagnosis of respiratory allergies.
• Detection of allergen-specific IgE.
The first method used for the measurement of serum allergen specific IgE has been the radioallergo sorbent test. This has been now replaced by immune-enzymatic methods.

- The measurement of serum-specific IgE is usually less sensitive than skin prick tests.
- The worst correlations between SPT and IgE assays are obtained with mold, food extracts and non-standardized extracts.

- But in general, the correlation between a strongly positive response to a skin test and the detection of serum-specific IgE and between a negative response to a prick test and the lack of detection of serum-specific IgE is very good.
In adults, levels of over 100-150 KU/l are considered to be above normal. Total IgE might be increased in other conditions such as smoke and parasitic diseases. Thus, the measurement of total-serum IgE should no longer be used for screening or allergy diagnosis.
• Allergen specific nasal challenge (ASNC)
• delivery of a small quantity of the allergen into one (or both) nostril, in order to elicit the allergic reactions, if allergen-specific IgE is present in the nasal mucosa

The main advantages of ASNC are
• the simplicity of execution,
• the low cost
• the safety.

Disadvantage the procedure is:
• still poorly standardized
• the technical details (amount of allergen, interval between doses, dilutions, positivity criteria) are largely variable among centres
• Indication
  a) to demonstrate the causal role of an allergen,
  b) to identify the clinically relevant allergen(s) in polysensitized subjects,
  c) to evaluate the effects of a treatment
  d) to study the inflammatory phenomena (Table 4)
  e) to evaluate the role of occupational allergens.
• CONTRAINDICATIONS
Acute bacterial or viral rhinosinusitis.
Acute exacerbation of allergic disease.
History of previous anaphylactic reaction
Severe general diseases
Pregnancy
Polyps
Recent ENT surgery (6-8 wks)
• **CAUSES OF FALSE POSITIVE**
  Nasal cycle
  Recent exposure to irritants
  Rhinosinusitis
  Priming effect

**CAUSES OF FALSE NEGATIVE**
Weak extract
Drugs
nasal antihistamine (1 day withdrawal)
oral antihistamine (3 day withdrawal)
nasal steroid (7 day withdrawal)
• Aspirin nasal challenge
• used to diagnose aspirin intolerance in the context of the aspirin hypersensitivity with respiratory manifestations.

The nasal challenge with aspirin was introduced later than the oral and bronchial challenge but has gained popularity since it rarely induces systemic reactions.

Nasal aspirin challenge is used in patients with severe asthma in whom oral or bronchial aspirin challenges are contraindicated.

The aspirin challenge is sufficiently standardized and reproducible
• the possibility of false negative results exist. For this reason, it is agreed that where an aspirin intolerance is suspected and the nasal challenge is negative, the oral challenge must be performed under medical supervision. Pulmonary function must be monitored during the challenge.

Oral, nasal steroids and antileukotrienes should be discontinued at least 7-3 days for antihistamines -- 24 hours for decongestants and cromones.
• Non-specific nasal challenges
• Nonspecific nasal reactivity is common in patients with allergic rhinitis

A wide variety of stimuli can be used to evoke nasal hyperreactivity.

These stimuli may directly act on a single receptor such as histamine, adenosine monophosphate, and methacholine, activate a more complex mechanism, such as mannitol, capsaicin, hyperosmolar solutions and cold air.

The results obtained with non-specific nasal challenges are often conflicting and difficult to interpret, due to the heterogeneity of methods, doses and outcomes.

Finally, the role of nonspecific hyper-reactivity in distinguishing different forms of rhinitis has not been established yet.

Use of non-specific tests is not essential for the clinical purpose and diagnosis of allergic rhinitis.
Assessing the sense of Smell

- Smell testing should be an integral part of the diagnostic approach in patients with smell dysfunction, i.e. hyposmia, parosmia or anosmia.

Several techniques are currently available for the objective evaluation of an individuals' smell capacity. The different tests that have been reported in the literature are:

- Connecticut Chemosensory Clinical Research Center Test (CCCRC)
- Smell diskettes test
- Odourant confusion matrix
- Dutch odour identification test (GITU)
- YN-odour Identification Test (YN-OIT)
- etc.. T&T Olfactometer
Assessing the Sense of Taste

• To evaluate the capacity of taste of five basic taste sensations, i.e. salt, bitter, sour, umami and sweet, in patients complaining of dysfunction of smell and taste.

Gustometry with application of taste substances and electrogustometry are the methods of taste examination. There are various ways of applying taste substances during gustometry examination.

• The stimuli used is citric acid or hydrochloric acid (sour taste), caffeine or quinine hydrochloride (bitter taste), sodium chloride (salty taste), saccharose (sweet taste), monosodium glutamate (umami taste).
• Electrogustometry estimating the functioning of taste by means of electric excitability thresholds determined through the response to the irritation of taste buds area with electrical current of different intensity. Electrogustometry is especially useful in estimating the efficiency of sensory pathways.
Nasal Nitric Oxide

- Nitric oxide (NO) is a colourless, odourless gas that is present in air exhaled through the mouth or nose.
- The role of NO in the airways is complex, possibly including antibacterial effects, pro-inflammatory effects, and regulation of blood flow and ciliary beat frequency.
• Exhaled NO (eNO) levels are raised in eosinophilic asthma and measurement of this has become a standardised, but not yet widespread, tool in diagnosis and management of asthma.

It can potentially provide a rapid, low cost, objective measure of lower airway inflammation.
Measurement of nasal NO (nNO) may represent a useful tool for research purposes as well as for screening for PCD. nNO in levels less than 100 ppb, particularly if these persist following decongestion, should stimulate investigation of mucociliary structure and function. Measurement may be a useful tool in the diagnosis and management of patients with chronic rhinosinusitis, nasal polyps, and CF.

Measuring both bronchial and nasal nitric oxide may assist the combined management of upper and lower airways.
Nasal Sampling: lavages, cytology, biopsies

• 1/Nasal blown secretions: secretions in the nasal airways are blown onto wax paper or a plastic wrap and then placed onto a glass slide. Microscopic evaluation allows the discrimination of epithelial cells from granulocytes.
• Nasal lavage. is the introduction of fluid into the nasal cavity and its recovery after a predetermined well time.

Nasal lavage is simple and rapid to perform, is well tolerated, and provides a sample that allows us to evaluate the content of the secretion in the nasal lumen such as protein, cells, mediators and cytokines.
• 3/Sinus packs or filter paper
  sinus packs are placed on the floor of the nasal cavity
  between the septum and inferior turbinate for 5 min
  and then placed back in a Falcon tube. In order to
  mobilize the nasal secretions out

If irritation of the nasal mucosa is an issue, thin filter
paper that can be inserted without touching the nasal
mucosa, can be used instead of sinus packs. The
amount of secretion that can be absorbed in this way is
however more limited
• 4/Microsuction technique

Nasal secretions can be collected by direct aspiration

advantages of minimal irritation of the nasal mucosa with the facility to determine concentrations per gram of secretion.
• 5/Nasal brush
small nylon brush used for cell sampling, is introduced in the middle meatus of the nose and turned carefully. The brush is immediately placed in a 5 ml polystyrene plastic tube

Nasal brush give information on living epithelial cells which is an advantage over nasal lavage, however the sampled area is smaller. Brushing can reliable to be used in babies and small children
6/Nasal scraping
Nasal scraping can be performed with the Rhinoprobe. The cupped tip of the disposable probe is gently passed over the mucosal surface of the medial aspect of the inferior turbinate.

Two or three short scrapes of the epithelial layer are made to obtain a sample.

- The specimen is spread onto a plain slide and immediately fixed

Nasal scrapings give information on living epithelial cells sometimes in larger lumps which is an advantage over nasal lavage,

however the area sampled is smaller than lavage and brush
• 7/Nasal biopsy specimens
   Biopsy specimens can be taken from the nasal mucosa, usually from the inferior turbinate. High quality 2.5-mm biopsy specimens can be taken under direct vision with nasal biopsy forceps, without visible damage to the epithelium of the sample and with sufficient depth of lamina propria

   Biopsies can be taken a number of times within one patient without causing significant problems
Evaluation of Nasal Patency

• Nasal patency can be monitored objectively by measuring the following parameters:

1/ nasal air flow passing through the nose during nasal respiration, evaluated with the nasal peak inspiratory and expiratory flow (PNIF and PNEF)

2/ the volume of the nasal cavity evaluated with acoustic rhinometry and

3/ the nasal airflow and pressure during nasal respiration evaluated with rhinomanometry.
1/Peak nasal inspiratory flow (PNIF)

- Nasal peak flow evaluation represents a physiologic measure of the air flow through both nasal cavities during forced inspiration and/or expiration expressed in liter per minute.

PNIF is the best validated technique for the evaluation of nasal flow through the nose.

Device:
Youlten peak flow meter (Clement Clark International) attached to anesthesia mask.
• Advantages
  - cheap and portable equipment
  - assistance not required after short training session (5 minutes)
  - rapid and easy to use
  - good correlation with subjective feeling of nasal obstruction

Disadvantages
  - influence of lower airway function
  - cooperation of patient required
  - no unilateral measurement possible
  - impossible in patients with alar collapse during inspiration
2/Rhinomanometry

- Active anterior rhinomanometry represents a physiologic measure of nasal air flow and pressure during normal inspiration and expiration. It is considered the standard technique for the evaluation of nasal airflow resistance, providing a functional measure of nasal patency each nostril separately.
Advantages
- specific measurement of nasal resistance
- information on each nostril separately
- relatively ease technique
- not time-consuming

Disadvantages
- relatively expensive equipment
- equipment not portable
- operator required
- impossible in case of total obstruction of one nostril
- interference with nasal cycle
- weak correlation with subjective nasal congestion
3/Acoustic rhinometry

- acoustic wave that is transmitted through a tube into one nostril
- The size and the pattern of the reflected sound waves provide information on the structure and dimensions of the nasal cavity,

The conversion of echo measurements to nasal volume requires mathematical calculations and theoretical assumptions.
• Advantages
  - easy to use
  - minimal patient cooperation
  - information of each nostril separately

• Disadvantages
  - non-physiological measure of nasal patency
  - operator required
  - interference with nasal cycle
  - weak correlation with subjective nasal congestion
Microbiology

• There is no evidence that microbiological assessment of nasal or sinus samples has any impact on outcomes in rhinitis/rhinosinusitis. Although randomized double blind placebo controlled trials indicate antibiotic treatment of ARS is significantly superior to placebo.

• There is no evidence that antibiotic treatment based on microbiological sampling gives better outcomes compared to empiric antimicrobial treatment in non-complicated acute rhinosinusitis.

Thus identification of pathogens in ARS is not indicated.
• European guidelines for the treatment of ARS suggest that ARS non-responsive to empirical antimicrobial treatment and topical nasal steroids, also complicated ARS, should be referred to an ENT specialist. At that time, further diagnostic including microbiology are advised.
Evaluation of Mucociliary Clearance

• 1/Mucociliary clearance time
• 2/Electron microscopy
• 3/Ciliary beat frequency measurement
• 4/Ciliogenesis in vitro
• Mucociliary clearance time:

The mucociliary transport (MCT) mechanism ensures the clearance of entrapped particles in the mucus lining the nasal mucosa towards the hypopharynx.

The saccharine test evaluates the time a patient needs to have a sweet taste after placement of a 1-2 mm particle of saccharine on the inferior turbinate mucosa 1 cm from the anterior end. The patient has to sit quietly with the head bent forward and without sniffing, coughing, sneezing, drinking or eating during the investigation.

The MCT is considered to be normal below 15 minutes, and should be less than 1 hour.
• MCT can only be measured in cooperative patients with patent nasal cavities and in the absence of severe mucosal disease,

This test has limited diagnostic value due to its low sensitivity and specificity. The test takes a long time and has a high incidence of false positive and negative results.
• Electron microscopy

Harvesting epithelial cells is performed by scraping along the inferior and middle turbinates by the use of a sterile cytology brush. These epithelial cells can be used for either structural investigation of the cilia of nasal epithelial cells with electron microscopy or for measuring ciliary beat frequency.

electron microscopic evaluation of harvested epithelial cells may aid in the diagnosis of PCD, but is not 100% sensitive nor specific.
Ciliary beat frequency measurement

Harvested epithelial cells can be evaluated of the frequency of the beating of cilia as well as the evaluation of their coordinated movement can be performed by computerized programs using a Fast Fourier analysis. The demonstration of normal CBF and beat pattern excludes the diagnosis of PCD.
Ciliogenesis in vitro:

The evaluation of ciliogenesis in vitro constitutes the gold standard for diagnosis of PCD, allowing the differentiation between primary and secondary ciliary dyskinesia.

A biopsy of the nasal mucosa is taken, and nasal epithelial cells are dissociated by enzymatic digestion and incubated for 6 to 8 weeks until cilia reappear on the apical side of the epithelial cells. The new cilia can be evaluated for their electron microscopic structure and coordinated activity. In PCD patients, no ciliogenesis takes place whereas patients with ciliary dysfunction due to infection/inflammation present with properly functioning ciliae after ciliogenesis.
• As these techniques are not available in routine ENT practice, one may rely on measuring nasal NO levels as low NO levels have been associated with PCD and therefore represent a good screening tool for PCD
Blood and Additional Tests

* full blood count including differential white cell count, ESR and/or C Reactive Protein,
* evaluation of renal, liver and thyroid function
* humoral immunity markers: immunoglobulins, IgG subclasses, specific antibody levels to tetanus, haemophilus, pneumococcus and response to immunization if low,
* cellular immunity markers: T and B cell numbers and ratios
* HIV status.
* Angiotensin converting enzyme (ACE)
* Anti-neutrophil cytoplasmic antibodies (ANCA)
Imaging in Rhinology:

1/Plain film radiographs provide little information on disease extent and no information on sinus anatomy.

- They do provide some information on the size of the sinuses and air content in the maxillary and frontal sinuses, but discriminate poorly between bone, mucosa and secretion compared to CT or MRI.
- may be misleading in diagnosis, dangerous in surgery.

Therefore, plain X-ray radiographs are not advised in routine rhinology clinic.

In children with clinical suspicion of adenoid hypertrophy being responsible for nasal obstruction, lateral plain X-ray images (Figure 15) may show the adenoid hypertrophy and be of help in the therapeutic approach in these children.
• 2/CT scanning has become the most important imaging modality helped the development of endoscopic surgery of the sinuses and skull base
• 3/MRI is recommended in patients with complicated inflammatory sinus disease extending beyond the boundaries of the sinonasal cavities and/or in patients with suspected neoplasms.
• 4/Ultrasonography of the paranasal sinuses easily available, cheap and quick, with no irradiation or discomfort involved.

Ultrasonography offers an opportunity for repetitive examination,

• Sensitivities have been reported from 29% to 100% and specificities from 55% to 99%

• limited to analysis of maxillary and frontal sinuses. However, it provides little information on disease extent
• Thank you