CLINICAL UPDATE

Chronic rhinitis in South Africa – more than just allergy!

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Chronic rhinitis is a troublesome condition for sufferers. It is tempting to label all patients with chronic nasal symptoms as having allergic rhinitis (AR), but many such patients have other causes of chronic rhinitis that need a specific diagnosis and management strategy. Even when the patient fully fits the definition of AR, their condition will be best served by combining medication with ongoing patient education.

S Afr Med J 2020;110(7):594-598. https://doi.org/10.7196/SAMJ.2020.v110i7.14553

The South African Allergic Rhinitis Working Group (SAARWG) turns 25 years old in 2020. We thought it would be appropriate to put out a consensus statement on important diagnostic and therapeutic principles that govern the diagnosis of allergic rhinitis (AR) and then suggest how the other common conditions that produce chronic rhinosinusitis should be entertained in the diagnosis and management of a patient with chronic nasal symptoms. Since its inception in 1995, the SAARWG has published eight statements on this condition.[1-8]

Definitions

AR is defined as inflammation of the nose due to sensitisation to allergens and is characterised by chronic nasal symptoms including nasal congestion, rhinorrhoea (anterior and posterior), nasal itch and bouts of sneezing.[9]

Chronic rhinosinusitis (CRS) is defined by the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS)[10] as inflammation of the nose and the paranasal sinuses characterised by two or more symptoms, one of which should be nasal congestion or nasal discharge, with changes on endoscopy and/or computed tomography.

The commonest reason for nasal and sinus symptoms is AR, which can usually be diagnosed on the basis of history and examination.[11] However, a common problem in South Africa (SA) is that patients (both adults and children) are not adequately diagnosed with AR, and in the absence of a supportive allergy test or failed therapy, or if additional symptoms are not present, the more common conditions in the differential diagnosis of CRS are frequently missed.

Diagnosing AR

The diagnosis of AR requires: (*i*) chronic nasal symptoms; and (*ii*) proof of systemic allergy. If testing is indicated, the favoured investigation is skin-prick testing for aeroallergens.

Laboratory allergy testing for AR in SA

In response to the overuse and incorrect use of laboratory testing for AR, in 2014 the SAARWG and the Allergy Society of South Africa (ALLSA), in consultation with the major private laboratories in SA, created a consensus diagnostic testing algorithm to simplify and standardise the process of specific immunoglobulin E (IgE) aeroallergen testing for the various regions of SA.[12] The consensus was based on review of allergy testing patterns and positivity over a 5-year period for all age groups, requested by general practitioners, specialists and allied health workers in different geographical regions of SA. This document and consensus led to some important changes in the practice of allergy testing. Chief among these was more cost-effective aeroallergen panels tailored specifically for SA, reducing costs for allergy tests by almost 50%, and greater use of individual-specific IgE tests, directed by the history, as opposed to pooled tests. Importantly, there was also a move away from total IgE as an entry point screening test for allergy.

However, recent analysis of laboratory data from one major private laboratory, after implementation of the consensus laboratory diagnostic approach, has shown that there is still a need for a better approach to allergy testing, requiring some changes to the existing consensus (Prof. E Vardas, personal communication, 2020) (Table 1).

The differential diagnosis of AR

When a patient has negative allergy tests or failed AR treatment, it is important to consider that the condition may not be AR. In descending order of importance, the following conditions need to be considered:

- Non-allergic rhinitis (n-AR)
- Idiopathic rhinitis
- Local AR
- Primary immunodeficiency diseases (PIDs)
- Cystic fibrosis (CF)
- Primary ciliary dyskinesia (PCD).

Non-allergic rhinitis

Table 2 lists the common types of n-AR, and Table 3 the differences between AR and n-AR.[13]

It should be remembered that a common cause of drug-induced rhinitis is rhinitis medicamentosa caused by abuse of topical intranasal decongestants.

Idiopathic rhinitis (vasomotor rhinitis)

Idiopathic rhinitis, or vasomotor rhinitis, is the most common cause of n-AR. This is a diagnosis of exclusion, and the condition is often difficult to manage. Common triggers include temperature changes, smoking, changes in barometric pressure or irritant exposures. Some patients with idiopathic rhinitis, especially those who have an eosinophilic inflammatory response, may respond to typical AR treatments, including intranasal corticosteroids and antihistamines.

Topical use of saline or Ringer's lactate douching may be appropriate. Capsaicin may be an appropriate therapy, but is currently unavailable in SA.[11]

Table 1. Continuing issues with allergy laboratory diagnostic testing in SA

- Continued inappropriate use of total IgE as a general allergy screen by general practitioners
- Over-use of pooled specific IgE screening tests for AR and food allergy, without breakdown, owing to funding restrictions or inadequate information given to patients about pooled screening tests
- Use of pooled aeroallergen screens tailored for the USA/Europe, which differ in content from SA recommended consensus panels
- Geographical localisation of allergens may not be necessary, and a single SA consensus algorithm needs to be developed
- Failure to tailor allergy testing to prevailing allergens (see 'Pollen calendars' below)
- Tree pollen testing under-represented in current consensus panel
- Inappropriate use of 'fx5' (paediatric food mix) for children aged >5 years and adults
- Food allergy testing for adults with isolated airway disease should be discouraged

SA = South Africa/n; IgE – immunoglobulin E; AR = allergic rhinitis.

Table 2. Causes of non-allergic rhinitis

- Hormonal rhinitis
- Drug-induced rhinitis
- Rhinitis of the elderly
- Gustatory rhinitis
- Occupational rhinitis
- Idiopathic rhinitis (vasomotor rhinitis/non-allergic rhinopathy)

Local AR

Local AR is a common condition in which systemic allergy testing is negative. Testing should include nasal provocation testing, but this is not commonly available in SA.

This condition responds well to common treatments for AR, intranasal corticosteroids and antihistamines.

The SAARWG recognises the difficulty of excluding idiopathic rhinitis and local AR, and because these conditions are fairly common, a trial of AR therapy may be appropriate.[11]

Primary immunodeficiency diseases

PIDs are more prevalent than was previously thought.[14] More than 350 forms have now been described, and almost all of them may involve the upper airway. PIDs present with either recurrence of acute infections or chronicity of infection. Otitis media and sinusitis are among the most frequent infections in PID patients. More than 40% of PID diagnoses are only confirmed in adulthood.[14]

Severe, persistent, unusual or recurrent upper airway infections should raise concern.[15] The Jeffrey Modell Foundation proposed specific warning signs of a possible underlying PID (Table 4).[16] Context is crucial in suspecting PID, and findings such as infections that are not limited to one organ system, infections that do not respond to standard treatment, or systemic features such as growth faltering, chronic fatigue, absenteeism, a family history of PID, etc. should prompt the clinician to perform at least first-line PID special investigations.

The first-line PID special investigations (Table 5) are helpful in screening possible cases.[17] More sophisticated (second-, third- or even fourth-line) investigations may be needed to define a specific PID form. These further investigations will require specific understanding, and referral to a specialist may be appropriate.

Cystic fibrosis

CF should be considered in a patient with the symptoms listed in Table 6. Appropriate testing for CF includes a sweat test and genetic testing.[18]

Primary ciliary dyskinesia

Although PCD is a rare disease, its prevalence can be substantial in patients with year-round nasal congestion that started before the age of 6 months, especially if other typical PCD symptoms are present.[19,20]

Both the American Thoracic Society[21] and the European Respiratory Society[22] recently published guidelines for the diagnosis and management of PCD. Although different diagnostic recommendations are made, both stress the need to increase the pre-test probability by including only patients who have common symptoms for diagnostic testing. Examples of such symptoms are listed in Table 7. Once the patient meets the clinical symptom score, recommended diagnostic tests are nasal nitric oxide, genetic testing, or both.[21,22] Electron microscopy of the nasal or bronchial mucosa can be valuable, but should only be performed in expert centres with well-trained staff to avoid poor-quality samples. Since these tests are not routinely available in SA, in their absence we stress that a clinical profile compatible with PCD, in a patient with recurrent 'sinobronchitis' and negative for PID or CF, should be diagnosed with PCD.

Endotypes of CRS

The need to define clusters of CRS through various biomarkers has become a special issue in medicine. To this end, two major categories of CRS have been defined. These are CRS with and without nasal

Table 3. Differences between AR and n-AR (modified from Greiwe and Bernstein[13])

AR	n-AR
• Usually presents in childhood	• Onset of symptoms later in life
• Strong family history of an atopic condition	• Negative family history
• Equal incidence in males and females	• More common in females
• Often seasonal exacerbations	• Little seasonal variation
• Positive allergy test	• Negative allergy test
• Aeroallergen triggers	• Irritant triggers
• Frequent eye symptoms	• Infrequent eye symptoms
• Frequent nasal itch	• Infrequent nasal itch
• Nasal mucosa oedematous	• Often clear watery secretions
• Frequent allergic 'shiners'	• Often normal face

AR = allergic rhinitis; n-AR = non-allergic rhinitis.

Table 4. PID should be considered in children and adults with the following clinical features (modified from Jeffrey Modell Foundation[16])

10 warning signs of PID in children	10 warning signs of PID in adults
1. ≥4 ear infections in 1 year	1. ≥2 ear infections in 1 year
2. ≥2 serious sinus infections in 1 year	2. ≥2 new sinus infections in 1 year in the absence of allergy
3. ≥2 months on antibiotic treatment in 1 year with little effect	3. One episode of pneumonia per year for more than 1 year
4. ≥2 episodes of pneumonia in 1 year	4. Chronic diarrhoea with weight loss
5. Growth faltering	5. Recurrent viral infections (colds, warts, herpes, condyloma)
6. Recurrent deep abscesses of the skin or other organs	6. Recurrent need for IV antibiotics
7. Persistent thrush or other fungal infections	7. Recurrent deep abscesses of the skin or other organs
8. Need for IV antibiotics to clear infections	8. Persistent thrush or other fungal infections
9. ≥2 deep-seated infections such as septicaemia	9. Infection with usually harmless bacteria like non-tuberculous mycobacteria
10. A family history of PID	10. A family history of PID

PID = primary immunodeficiency disease; IV = intravenous.

Table 5. First-line special investigations for screening for possible PID

Investigation	Comment
1. Appropriate investigations to exclude HIV infection and other causes of secondary immunodeficiencies	Secondary causes of immunodeficiency are more prevalent in SA than PID
2. Full blood count and differential count	Lymphopenia and neutropenia may indicate a PID Recurring cytopenias should raise concern
3. Calculated globulin	A decreased calculated globulin (serum protein minus serum albumin <18 g/L in adults) may indicate a reduction in immunoglobulin production
4. Serum IgG, IgM and IgA	Evaluation of immunoglobulin quantity Hypogammaglobulinaemia of specific importance Refer to interpretation in different PID forms
5. Serum IgE	Very increased serum IgE values may be an indication of PID rather than allergy
6. Antigen-specific IgG (vaccine antibodies): tetanus IgG and pneumococcal serotype IgG	Evaluation of immunoglobulin production quality Baseline values must be interpreted in relation to age and vaccination status Cannot be interpreted after recent immunoglobulin administration Appropriate revaccination and response measurements may be indicated Interpretation requires a specific understanding
7. Total complement activity	

PID = primary immunodeficiency disease; SA = South Africa; Ig = immunoglobulin.

polyps. CRS is also classified into eosinophil-driven and neutrophil-driven disease with separate cytokine profiles.[23]

There are regional differences in CRS, with Caucasians and African Americans having predominantly eosinophilic disease and Asians predominantly neutrophilic disease. However, Asians in the USA have a higher proportion of eosinophilic disease, and disease patterns in Asia are changing. There is a lack of data for Africa.

Using these endotypes for personalised medicine is now a reality.[24]

Surgical alternatives in CRS

Some patients who have CRS and fail topical therapy may need further investigations and possibly surgical treatment. These conditions are listed in Table 8.

Pollen calendars and pollen counts in SA

SA now has seven city pollen monitoring sites that report weekly changes in pollens and mould spore counts by region. These counts will inform allergy testing panels for AR and allergic asthma and should inform decisions on responses to environmental changes brought about by population movements and climate change (visit https://pollencount.co.za).

Infectious rhinitis

Most upper respiratory tract infections are viral, and antimicrobial stewardship principles in SA suggest that antibiotics should not be used for common 'colds'.[25]

Treatment of AR

The correct treatment of AR involves regular use of a topical corticosteroid nose spray on a daily basis, occasional use of a non-sedating antihistamine, and careful and limited use of topical nasal decongestants. For patients with avoidable triggers, these should be avoided, and for patients whose condition is more severe, specific and sublingual immunotherapy are very useful therapeutic options.

Patient education and empowerment

Poor adherence to therapy and inadequate techniques of using medication are major factors preventing adequate control of AR symptoms. A critical and missing step in the management of AR is ensuring that patients use their therapy correctly. Because this step is so important, we suggest that all healthcare practitioners should educate patients and the parents of children in whom they make the diagnosis of chronic rhinitis and prescribe medication.[11]

Education should include the following important points:

- AR is a chronic disease that requires regular controller therapy.
- Patients should recognise less frequently perceived symptoms of AR such as blockage and be empowered to more accurately assess the control of their symptoms.

Table 6. Features of cystic fibrosis

- Upper respiratory tract symptoms: nasal obstruction and posterior/anterior nasal discharge
- Recurrent sinusitis and opacification of sinuses on radiological testing
- Nasal polyposis
- Recurrent serous otitis media and persistent otorrhoea following drainage tubes
- Especially in the context of recurrent lower respiratory tract and gastrointestinal symptoms

Table 7. Clinical features of primary ciliary dyskinesia[19,20]

- Neonatal respiratory distress
- Organ laterality defect
- Recurrent otitis media with effusion
- Year-round daily cough
- Year-round daily nasal congestion
- Chronic pansinusitis
- Recurrent lower respiratory tract infections
- Bronchiectasis
- Male infertility

Table 8. Conditions causing upper respiratory tract symptoms that usually need surgical correction

- Septal deviation
- Concha bullosa deformity and other turbinate disorders
- Sinusitis including fungal sinusitis
- Nasal valve collapse
- Chronic tonsillitis
- Adenoidal hypertrophy
- Tumours

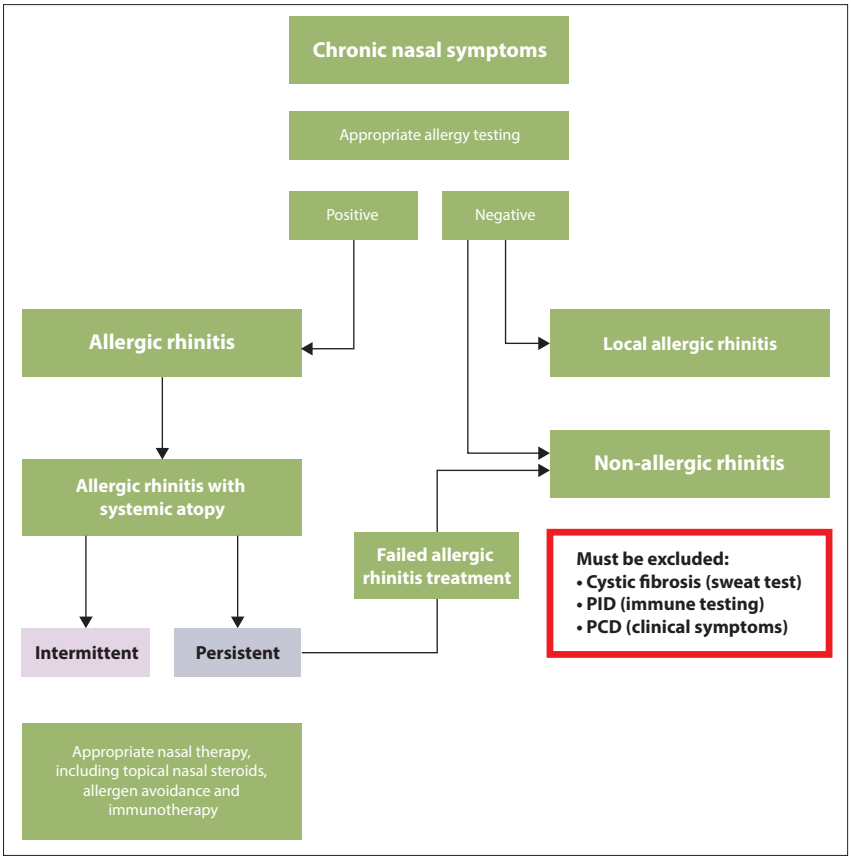

Fig. 1. Summary of an approach to chronic nasal symptoms. (PID = primary immunodeficiency disease; PCD = primary ciliary dyskinesia.)

- Technique of administration of intranasal corticosteroids must be optimal to ensure symptom control.

Assessment tools may allow more effective management of AR. The Medication Adherence Report Scale (MARS) is a 5-item tool that assesses adherence to therapy.[26] A simple approach to assessing adherence is always to ask patients how often they forget to take their medication, instead of asking how often medication is given.

Assessment of patient quality of life is an important part of the assessment of AR impact on patients, and especially in assessing medication benefit.[11]

The Rhinitis Control Assessment Test (RCAT) is a self-assessment test using a 5-point frequency scale.[27] The test has been well validated, and a score of ≤21 has been proposed as indicating poor control; however, it has never been studied in children aged <12 years. As in asthma control, the appropriate response to poor control is to first reassess the diagnosis, look for concomitant conditions, exclude ongoing exposure to irritant and allergic triggers, and ensure adequate adherence and technique before increasing therapy if necessary.

The technique of using intranasal medication is critical to ensure adequate deposition on the turbinates, as well as to avoid deposition in the anterior nasal space or on the septum. The nose should be clear of all secretions prior to administering a nasal spray, by blowing the nose, performing nasal lavage, or both.

Conclusions

The SAARWG celebrates 25 years of contributing to the management of AR. The Working Group consider that AR management should include the following key principles, outlined in Fig. 1:

- Adequate diagnosis
- Appropriate use of medication, especially intranasal corticosteroids
- Appropriate patient education and advice
- Trial of therapy for no more than 3 months, and if there is no response proceed to investigating for PID, CF or PCD.

Declaration. None.

Acknowledgements. None.

Author contributions. All authors contributed equally to the data and write up. RJG wrote the final manuscript.

Funding. None.

Conflicts of interest. None.

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Accepted 3 March 2020.