One airway, one disease

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Allergic rhinitis (AR), the most common immunological disease, remains under recognised and poorly managed with an under-appreciated socioeconomic impact.[1,2] AR and chronic rhinosinusitis (CRS) impacts quality of life (QoL) not only because of the physical discomfort, but also because of the associated detrimental effects on the psychological and social aspects of patients' lives, such as interference with intellectual performance and productivity at work and school.[3] During the allergy season, people with AR show declines in cognitive processing, psychomotor speed, verbal learning and memory[4], in addition to sleep deficits and an increased risk of traffic accidents.[3] These undermine an individual's QoL, particularly when the AR is untreated or poorly managed.

Numerous patient and healthcare professional (HCP) factors contribute to this under-recognition and poor management. Patients and HCPs may dismiss AR as little more than a nuisance.[2] To exacerbate the clinical problem, diagnosing and treating AR can prove challenging.[2] However, even when accurately diagnosed and well-managed, patients tend to be poorly adherent to treatment, generally self-medicate and use on-demand treatment when symptomatic.[5] As this behavioural pattern suggests, many AR patients follow neither guidelines nor their prescription instructions[5] and do not seek further review after diagnosis. Clinicians need to be vigilant that AR does not mask an underlying serious condition and actively seek red flags at each review.

AR is not, however, a discreet disease. The respiratory tract runs continuously from the nasal vestibule to the alveoli.[6] Until the late 1990s, anatomists used structure and function to delineate the respiratory tract into the upper (nasal cavity, pharynx and larynx) and lower (trachea, bronchi, bronchioles and alveoli) airways.[7-9] Similarly, most clinicians diagnosed and managed asthma and AR as distinct clinical entities affecting the upper or lower airways respectively.[7] Indeed, considerable epidemiological, pathophysiological and clinical evidence now suggests that the upper and lower airways are a single functional and morphological unit, [8,10,11] which promoted Interasma (Global Asthma Association) to publish a manifesto stressing that patients with 'United Airways Diseases', such as AR, nasal polyposis and asthma, need "timely and adequate diagnosis, treatment, and, when recommended, referral for management in a specialized center".[12]

According to the so-called 'one airway, one disease' view, asthma, polyposis, AR and other diseases are on "a continuum of inflammation" within one airway.[7] This document summarises the implications of this 'one airway, one disease' view for primary care HCPs and patients. Our intention is for the upper airways to be considered in tandem with the lower airways to avoid misdiagnosis and undermanagement.

The complexity of rhinitis

Rhinitis refers to inflammation of the nasal mucosa.[1] Clinically, patients experience nasal discharge, itching, sneezing and blockage or congestion of varying severity and frequency (Table 1).[1,13] Behind this relatively simple symptomatic presentation lies a disease of remarkable complexity. There are several types of rhinitis, typically divided into: AR; non-allergic rhinitis (NAR); infective (see below); and mixed.[1]

Table 1: The ARIA classification of AR[13]

Characteristic	Definition
Intermittent	Symptoms are present for fewer than 4 days a week or for fewer than 4 consecutive weeks
Persistent	Symptoms are present for more than 4 days a week and for more than 4 consecutive weeks
Mild	Patient does not experience any of the following: • Sleep disturbance • Impairment of daily activities, leisure and/or sport • Impairment of school or work • Symptoms present but not troublesome
Moderate/severe	Patient experiences one or more of the following • Sleep disturbance • Impairment of daily activities, leisure and/or sport • Impairment of school or work • Troublesome symptoms

Numerous lines of evidence support the "one airway, one disease" concept. Common inflammatory mediators, some disease susceptibility genes and pathophysiological profiles seem to underlie asthma, AR and CRS.[8,11] The same factors (eg house dust mite faeces, fungi, saliva and urine of domestic animals and pollen) can trigger AR and asthma.[3]

Asthma patients with AR tend to show worse disease control and more intense airway inflammation than those with asthma alone.[8] Indeed, untreated or poorly managed rhinitis can increase the risk of an asthma exacerbation.[3] In asthma patients, CRS is associated with exacerbations, poor disease control, airflow limitations and elevated blood and sputum eosinophil counts and fractional exhaled nitric oxide (FeNO) levels.[8] This overlap underscores the importance of especially close monitoring and follow up of asthma patients with AR to optimise management of both conditions.

In line with the 'one airway, one disease' concept, the nature of inflammation in the upper and lower airway is usually

Figure 1. A cascade of inflammatory mediators causes allergic reactions[45]

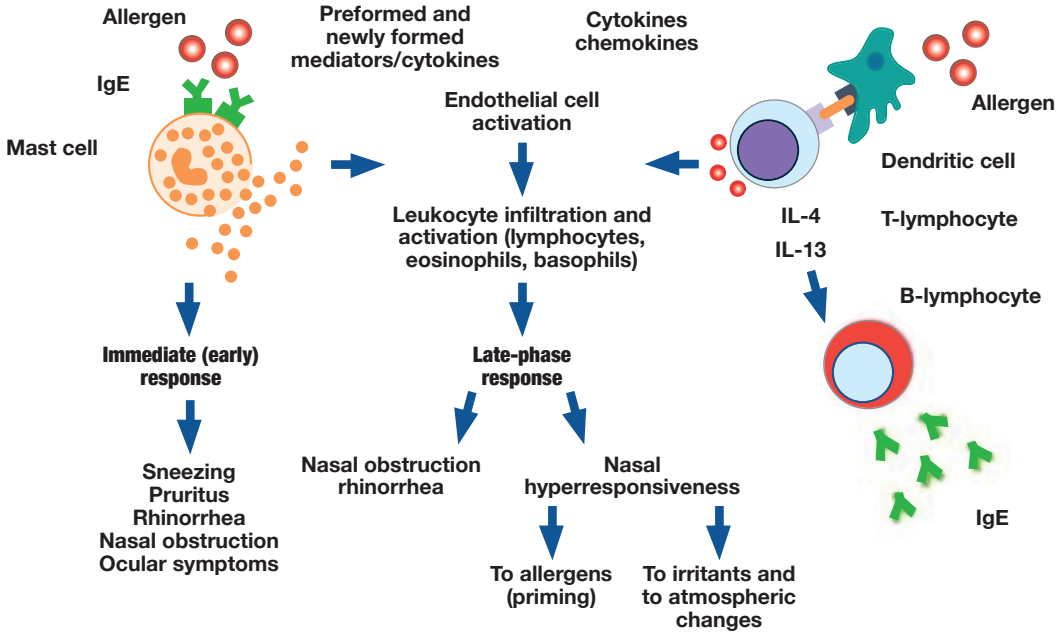


Image adapted from Dhruve[45]

Table 2: "Red flags" and other indications for ENT referral[1,35]

Speciality	Indication for referral
Red flags	Heavily blood-stained nasal discharge
	Nasal pain
	Recurrent epistaxis
	Unilateral symptoms
Other indications	Nasal blockage inadequately relived by drug treatment
	Structural deviations (eg septal deviation) that make drug treatment difficult

the same.[8] Allergen challenge in the nose causes allergic inflammation in the bronchus and vice versa, while leukotrienes are inflammatory mediators in asthma and AR.[8] In addition, common immunological pathways seem to link asthma with CRS with nasal polyps (CRSwNP), including those involving interleukin (IL)-4 and IL-13.[8] Eosinophilia in peripheral blood, which indicates systemic inflammation (figure 1), is often identified in AR and asthma.[14] Biopsies from people with asthma can show raised levels of eosinophils in their nasal mucosa without developing symptoms of rhinitis.[14,15] Such immunological insights can guide management.

In line with the 'one airway, one disease' concept, type 2 inflammation affecting the terminal and respiratory bronchioles occurs in asthma and AR.[11] Overactivity of T_H1, T_H17 (which target intracellular and extracellular pathogens respectively) or both seem to contribute to autoimmune disease and, in the case of T_H1 cells, chronic inflammation. T_H2 lymphocytes, part of the type 2 inflammatory response, protect against parasitic helminths and drive allergies.[16] Patients with asthma, AR or CRS can all show local mucosal immunoglobulin E (IgE). This antibody, in turn, activates eosinophils and mast cells to tackle helminths.[6,16] The presence of IgE can aid the differential diagnosis of asthma and AR, but is not definitive.[1,17]

Epidemiology

Epidemiological studies also support the 'one airway, one disease' concept. In the UK, between 10% and 15% of children as well as 26% of adults have AR.[1] The incidence of AR rises from 3.4% of 4 year olds to 27.3% of 18 year olds.[18] Before adolescence, boys are more likely to present with rhinitis than girls. After adolescence, rhinitis is more common among females.[1] Based on nine studies, Settipane estimated that there are three AR cases for each NAR case.[19]

The prevalence of diagnosed AR in the UK increased markedly between 1971 and 1991, although this rise may have plateaued or declined in recent years.[1,20] While genetic predisposition is important in rhinitis development, classical evolution is too slow to account for the rapid rise.[1] Therefore, environmental factors (eg smaller family size, urban environments and reduced exposure to parasites and other infections) are important factors underlying the rise.[1]

Globally, an estimated 262 million people had asthma in 2019, which accounted for 461,000 deaths.[21] In England, 17% of men and 18% of women aged 16 years and older interviewed during 2018 had received an asthma diagnosis.[22] Moreover, 12% of boys and 7% of girls had been diagnosed with asthma.[22] As this study[22] shows the prevalence of asthma can vary widely even in the same country. Asthma UK estimates, however, that 5.4 million people in the UK are currently receiving treatment for asthma,[23] which may suggest considerable undertreatment. An estimated 10.9% of the European population have CRS.[24] In this study, which used postal questionnaires, smokers were 70% more likely to developing CRS than non-smokers.[24]

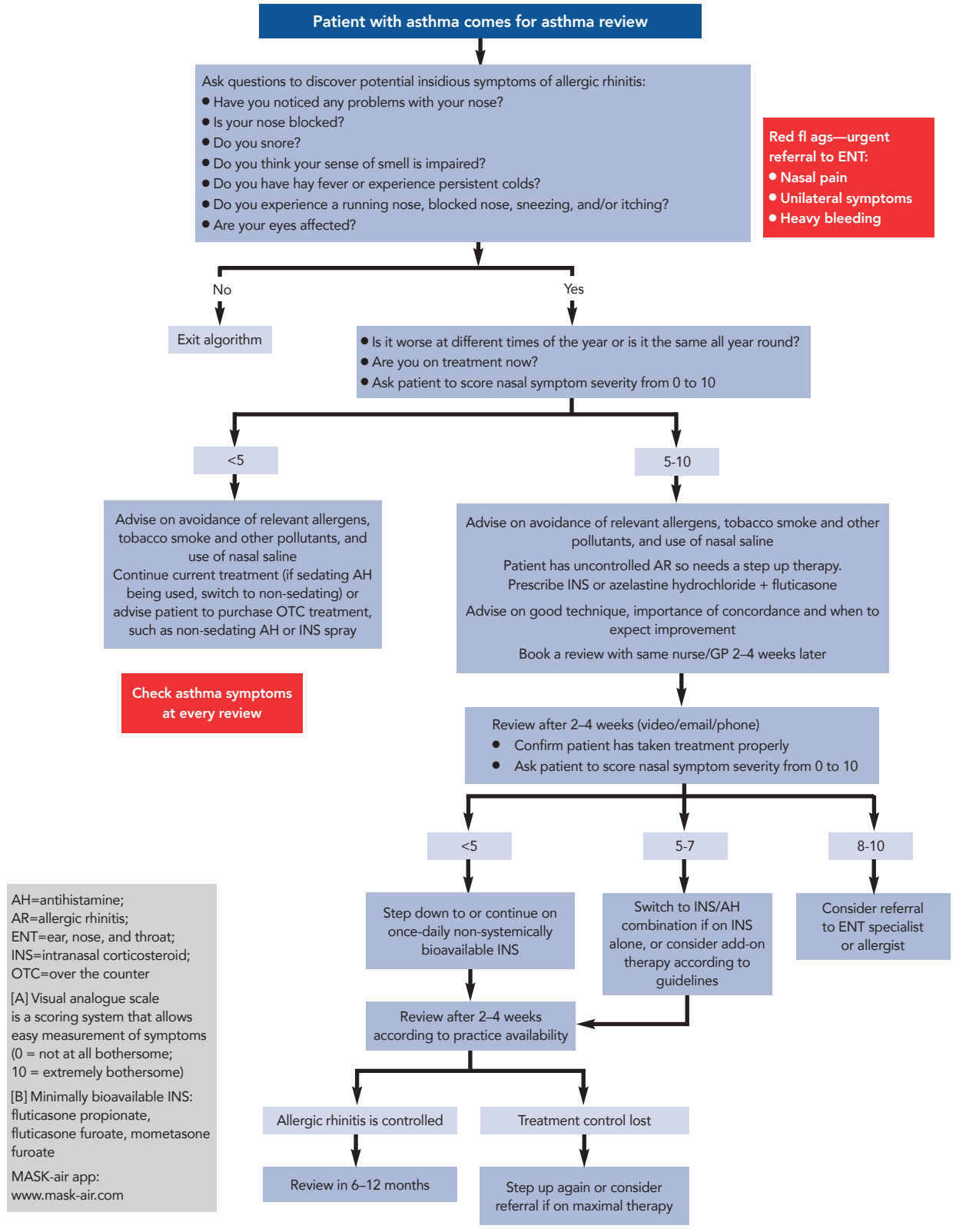
Differential diagnosis

History, examination and, when necessary, specific allergy tests are the foundation of AR diagnosis, but the differential diagnosis can be challenging. HCPs also need to be vigilant for red flags. For example, patients with unilateral symptoms, heavily blood-stained discharge or pain should be referred to ENT.[1] Table 2 summarises some red flags that should alert clinicians to potentially important other causes that could warrant specialist referral. Nevertheless, patients still require treatment to reduce the risk of needing an acute admission, while waiting for the ENT appointment. Figure 2 offers an algorithm summarising the diagnosis and management of AR in people with asthma.

Allergic rhinoconjunctivitis

During the diagnosis, HCPs should consider the extent and presence of rhinorrhoea and crusting.[1] Unilateral rhinorrhoea (table 3) is uncommon and, because of the risk of cerebrospinal fluid (CSF) leak, is a red flag.[1] Severe crusting also requires further investigation.[1] intranasal steroids do not normally cause crusting.[1] Common differential diagnoses in primary care include:

Figure 2. Identifying and managing AR in the asthma population[46]



The suggestions in this algorithm are informed by evidence-based guidance.

Table 3: Interpreting rhinorrhoea[1]

Colour	Interpretation
Continuously clear	Infection unlikely; secretions are clear in early viral rhinitis
Unilateral and clear	Exclude CSF leak
Yellow	Allergy or infection
Green	Usually infection; secretions may show small amounts of blood
Unilateral and coloured	Tumour, foreign body, nose picking or nasal spray misapplication
Bilateral and coloured	Nasal spray misapplication, granulomatous disorder, bleeding diathesis, infection, nose picking

- Chronic rhinosinusitis[1]
- Nose picking[1]
- Granulomatous polyangiitis[1]
- Sarcoidosis or other vasculitides (particularly with bleeding)[1]
- Cocaine abuse[1]

Visual inspection and anterior rhinoscopy can aid the differential diagnosis (tables 4 and 5).[1] Partial or complete nasal obstruction is common among AR patients. The severity often correlates with systemic allergic signs and symptoms.[1] Nevertheless, obstruction can arise from numerous causes other than rhinitis (eg septal deviation, foreign body, tumours and nasal polyps),[1] which should be considered during the differential diagnosis. HCPs should remember that small polyps and those confined to the sinuses can be difficult to observe using anterior rhinoscopy[1] and may not cause total obstruction. Anterior rhinoscopy readily reveals larger polyps in the nasal vestibule, which can extend to the nares. HCPs can distinguish polyps from inferior turbinate by: lack of pain and sensitivity when touched and being able to get between the polyp and the wall of the nostril.[11]

As mentioned, the 'one airway' means that AR patients often develop lower respiratory tract symptoms, including cough, wheeze and dysponea.[1] Rhinitis patients can present with a range of other symptoms including:

- Snoring and other sleep problems[1]
- Repeated sniffing[1]
- Nasal intonation[1]
- Pollen-food syndrome (cross-reacting antigens in some fruits, vegetables and nuts).[1]

AR is also associated with co-morbidities, which HCP should consider during the differential diagnosis, such as:

- Asthma and other allergic diseases[1]
- Rhinosinusitis[1]
- Hyposmia (loss of smell)[1]
- Middle ear, throat and laryngeal problems[1]
- Chronic obstructive pulmonary disease (COPD): About 30% of COPD patients suffer from AR. Moreover, COPD seems to be a risk factor for non-infectious rhinitis.[12]
- Obstructive sleep apnoea and sleep-related breathing disorder.[1,12]
- Ocular involvement can produce itching, redness and swelling of the conjunctiva, watering and lid swelling. Eye rubbing exacerbates periorbital oedema.[1]

As part of the diagnostic work up, HCPs should consider exposure to pets and other animals, and whether certain medicines (eg alpha and beta-blockers, other anti-hypertensives, aspirin and other non-steroidal anti-inflammatory drugs, oral contraceptives and topical sympathomimetics) could cause or aggravate rhinitis.[1]

Patients may need referral for nasal endoscopy if there is diagnostic ambiguity.[1] HCPs could consider referral for skin prick tests (SPTs), measurement of specific IgE or both. For instance, patients with rhinitis symptoms, but without identifiable allergic triggers and who are negative for systemic IgE may have NAR.[1] On the other hand, at least 15% of people with a positive skin prick test do not develop symptoms on exposure to the allergen.[1] Serum-specific IgE may be useful when SPT are not possible or when the SPT and clinical history are equivocal.[8]

FeNO testing may also aid the differential diagnosis of AR and asthma, and appears to be a prognostic indicator in asthma.[25,26] Haccuria *et al* reported that after using saline to induce sputum, the mean decrease in FeNO was not significantly different (p=0.447) in people with asthma (55.1%; n=31) compared with those with AR (50.0%; n=23). The decline in people with asthma (p=0.007) and AR (p=0.029) greater than in controls (40.8%; n=24).[11] The finding suggests that type-2 inflammation contributes to both diseases.[11] Normal levels are less than 20 ppb, but become elevated in eosinophilic lower respiratory tract inflammation.[1]

Non-allergic and occupational rhinitis

NAR is a diagnosis of exclusion, which HCP should consider in patients with nasal symptoms and negative SPT.[1] NAR may

Table 4: Interpreting visual assessment

Observation	Interpretation
Allergic salute	Supports AR diagnosis
Horizontal nasal crease across nasal dorsum	Supports AR diagnosis
Conjunctivitis and other eye involvement	Bilateral, non-sticky conjunctivitis that is associated with other symptoms supports AR diagnosis; Unilateral conjunctivitis, sticky eyes or reduced visual acuity should warrant further assessment
Chronic mouth breathing	Several causes need consideration, especially in children, including enlarged tonsils, habitual mouth breaking and, mainly, causes of blocked nose
Allergic shiners	Supports AR diagnosis, but a non-specific appearance may indicate other causes of oedema
Assessment of nasal airflow (eg metal spatula misting)	Supports a diagnosis of nasal blockage with many potential causes (eg allergic and non-allergic AR; foreign body, tumour)
Depressed nasal bridge	Post-surgery, granulomatous polyangiitis, cocaine misuse, infections (eg syphilis, leishmaniosis, leprosy), racial background
Widened nasal bridge	Polyps and nasal polyposis
Changes to nasal appearance	Sarcoidosis (purple nasal tip); seborrhoeic dermatitis (nasal crease); rosacea (phymatous changes)

Based on Scadding *et al*[1]; Andrade *et al*[41]; Park *et al*[42]; Zhang *et al*[43] and the authors' clinical experience and expertise

Table 5: Interpreting anterior rhinoscopy

Finding	Interpretation
Hypertrophic, pale and boggy inferior or middle turbinates	Inflammation (nasal appearance may be normal in AR); Nasal polyps are usually described as boggy and non-tender; middle turbinates are very sensitive if touched
Presence or absence of clear, coloured or purulent secretions	See table 1
Deviated septum	Unlikely cause of rhinitis, although deviated nasal septum and AR are both common
Presence or absence of nasal polyps	Polyps and nasal polyposis
"Cobblestone" yellow submucosal nodules	Sarcoidosis (Rare presentation)
Crusting and granulations	May suggest infection and, possibly vasculitis
Septal perforation	Septal surgery, chronic vasoconstriction (cocaine, alpha agonists), granulomatous polyangiitis, anti-phospholipid antibody syndrome and nose picking

Based on Scadding *et al*[1] and the authors' clinical experience and expertise

be the presenting symptom for certain rare but important systemic disorders (eg granulomatous or eosinophilic polyangiitis, and sarcoidosis).[1] Clinicians should, therefore, always consider alternative diagnoses.

Occupational rhinitis is 2 to 3 times more common than, and often precedes, occupational asthma.[1] Occupational asthma and occupational rhinitis often co-exist.[1] The diagnosis of occupational rhinitis depends on a detailed history, which a symptom diary facilitates. The diary can, for example, determine seasonality and whether the symptoms occur indoors, outdoors or both. Occupational rhinitis may improve at weekends and during holidays.[1] Many people with occupational rhinitis do not, however, improve as the inflammation often take time to abate in the absence of the allergen.

The symptom pattern may also indicate possible triggers.[1] Over 300 factors can, however, cause occupational rhinitis including protein allergens derived from plants or animals, for example, flour, latex and laboratory animals.[1] So, unless other factors suggest a cause, referral for testing SPT and measurement of specific IgE is impracticable. Removing a possible allergen from the individual's environment or vice versa can help confirm the diagnosis.[3]

Viral triggers

Viruses, and less commonly bacteria, fungi and protozoa, cause infective rhinitis by triggering congestion of the nasal mucosa. The congestion, in turn, can occlude the sinus ostia, which predisposes to acute rhinosinusitis, Eustachian tube dysfunction or both.[1]

Children

In general, the approach to diagnosis is similar to that in adults: history, SPT and anterior rhinoscopy. HCPs should refer children with entopy (local allergic rhinitis) for nasal allergen challenge.[1] Acute viral rhinitis is common in children, particularly during the winter. Most children experience up to 10 episodes per year. The number of cases peaks between 6 months and 6 years of age. After this age, children typically experience 1-2 episodes a year, mainly during the winter.[1] HCPs should also consider whether retained foreign body, nasal septum deviation, unilateral choanal atresia, cerebrospinal fluid leak and nasal polyposis could cause rhinitis[1] and refer as appropriate.

Chronic infective rhinitis (rhinosinusitis) persists for more than 3 months and, particularly if severe, can be a manifestation of underlining pathologies such as primary ciliary dyskinesia, cystic fibrosis or antibody deficiency.[1] These children may require referral to clarify the diagnosis. AR may also be associated with otitis media with effusion, adenoidal hypertrophy or both. Some studies suggest that treating rhinitis improves otitis media with effusion and adenoidal hypertrophy.[1]

AR often presents alongside other atopic disorders, especially asthma, eczema and food allergy. Conjunctivitis, impaired hearing, rhinosinusitis, sleep problems, pollen-food syndrome and other co-morbidities may influence presentation among children.[1] In addition to increasing the risk of asthma, AR can adversely impact children's QoL and can have detrimental effects on sleep, behaviour, school performance and family dynamics.[1]

Treatment

Allergen and irritant avoidance

HCPs should suggest allergen avoidance as the cornerstone of treatment, even though this often proves difficult to implement in practice and many of the studies are small and methodologically poor.[1] HCPs should also considering advise rhinitis patients to avoid, where possible, irritants, including smoke and traffic pollution.[1] In line with the 'one airway, one disease' concept smoke and traffic pollution also exacerbate and contribute to asthma.[27,28]

HCPs can suggest that people with allergies to animals limit their exposure as far as possible.[1] People with allergies to house dust mite could consider allergen-impermeable bedding and using acaricides on carpets and soft furnishing.[1] In addition, the following measures may help reduce allergen exposure in people allergic to pollen:

- Sunglasses, nasal filters, balms and ointments applied to the nose may reduce exposure to pollen,[1] possibly by providing a physical barrier.
- Nasal irrigation using isotonic saline in adults and children with AR is well tolerated, inexpensive and simple to use, alleviates symptoms and reduces the amount of pharmacotherapy.[1,29]
- Avoiding outdoor activity when pollen is highest, such as during the early morning and evening, and mowing[1]
- Avoiding outdoor activity during and after thunderstorms,[1] especially in summer when high levels of pollen are airborne
- Timing holidays to avoid the pollen season[1]
- Keeping house and car windows closed,[1] during the season when the pollen count is high
- Shower and wash hair after high exposures[1]
- Avoid drying washing outdoors when the pollen count is high[1]; pollen can become trapped on fabrics

In addition, HCPs should suggest starting treatment two weeks before a known allergen season to optimise efficacy.[1]

Drug treatments

Medication is appropriate if patients experience persistent symptoms despite making best efforts to avoid allergens and irritants.[1] The symptom pattern guides the choice and HCPs should ask which previous treatments for rhinitis worked and which did not.[1] Patient preferences, availability and cost also influence treatment choice.[30] In line with the 'one airway, one disease' concept, several drugs are active in asthma and AR.[7,8]

Acknowledging the relationship of asthma and AR is of importance in the rationale of treatment. Even in the absence of AR, rhinitis strongly predicts adult-onset asthma.[31] Furthermore, treating AR in patients with mild to moderate persistent asthma resulted in a progressive and significant decrease in nasal and pulmonary symptoms and asthma-related morbidity, absence from work, emergency department visits and night-time awakenings.[32]

Table 6: Examples of first and second generation anti-histamines[44]

Generation	Example
First-generation (should not be used in allergic rhinitis because of risk of drowsiness)	Brompheniramine
	Chlorpheniramine
	Dexchlorpheniramine
	Hydroxyzine
	Ketotifen
	Promethazine
Second-generation	Cetirizine
	Desloratadine
	Ebastine
	Fexofenadine
	Levocetirizine
	Loratadine

Antihistamines

Antihistamines, which are available as oral, intranasal and ocular formulations, are effective in AR. The choice depends less on clinical efficacy and more on the differences between adverse events and the clinical situation (eg pregnancy and breastfeeding).[1] One potential argument against a single airway concept is that intranasal and oral antihistamines work for AR but are, in most clinical studies, ineffective in asthma.[1,33] Nevertheless, some authors speculate that H_1- and H_4-antihistamines may be clinically effective in some asthma subtypes.[33] This hypothesis requires confirmation in robust clinical studies.

Oral H_1-antihistamines reduce mean daily rhinitis symptom scores (in absolute terms) by an estimated 7% compared with placebo and can significantly improve QoL.[1] Oral H_1-antihistamines also reduce histamine-driven symptoms (eg itch) at sites other than the nose, such as conjunctiva, palate and skin.[1] Patients with persistent rhinitis may need regular rather than "as needed" use.[1] Monotherapy with oral H_1-antihistamines is associated with poorer control than intranasal corticosteroids (INS).[1,5]

First-generation oral antihistamines (table 6) can cause sedation and impair cognition, which can undermine driving ability and examination results, which are also impaired by rhinitis.[1] The BSACI guidelines does not recommended first-generation antihistamines.[1]

Although individual susceptibility varies, second-generation oral antihistamines (table 6) are long acting, generally non-sedating and have no clinically significant anti-cholinergic activity.[1] The latter may be a consideration given the association between anti-cholinergic burden and cognitive and physical impairment in later life.[34] Nevertheless, second-generation oral antihistamines may have adverse events and interactions that influence the choice for specific patients.[1] HCPs should review the electronic Medicines Compendium before prescribing any medication.

Nasal antihistamines are more effective than oral formulations at reducing rhinitis symptoms and nasal obstruction, and act more rapidly (within 15 minutes) allowing use as rescue therapy. Nevertheless, continuous use is more effective than on-demand treatment. Nasal antihistamines do not, however, improve histamine-related symptoms at other sites (eg skin), and may cause local nasal irritation.[1]

The BSACI guidelines suggest that oral antihistamines are the first-line therapy for mild-to-moderate intermittent and mild persistent rhinitis (table 1).[1] Oral antihistamines can also be added to INS when moderate and severe persistent rhinitis is inadequately controlled on the latter alone especially when the patient has ocular symptoms. Nasal antihistamines are the first-line therapy for mild-to-moderate intermittent and mild persistent rhinitis and are appropriate for moderate and severe persistent rhinitis that is inadequately controlled on INS alone.[1]

The BSACI guidelines suggest mast cell stabilisers (eg sodium cromoglycate, nedocromil sodium and lodoxamide) as the first-line treatment for ocular symptoms. Some patients, however, prefer antihistamines, such as azelastine, emedastine and epinastine.[1] Olopatadine, which shows mast cell stabilising and antihistaminic properties, is often effective, is well tolerated and is applied twice daily, which particularly suits contact lens wearers.[1]

Oral corticosteroids

Oral steroids are rarely indicated in AR.[1] Oral steroids may be useful in specific circumstances, such as short-courses before a wedding. Occasionally, oral steroids may be appropriate for chronic rhinosinusitis with nasal polyposis associated with severe inflammation.[1] HCPs can consider a short-course of oral steroids (0.5 mg/kg in the morning for 5–10 days) for adults with severe, uncontrolled symptoms that significantly affect quality of life.[35] Oral steroids should be prescribed as the shortest course at the lowest dose that adequately controls symptoms, because of the risk of side-effects including infection, venous thromboembolism, avascular necrosis, and fracture, diabetes mellitus, hypertension and osteoporosis.[36] In general, depot steroid injections should be avoided unless there is no alternative treatment.[37]

Nasal corticosteroids

INS are the main anti-inflammatory for AR.[1] Some cases of NAR are eosinophilic and may, therefore, respond to INS.[1]

According to BSACI guidelines, INS are the treatment of choice for moderate to severe persistent AR. If monotherapy fails to adequately control symptoms, INS plus intranasal antihistamine is more effective than either alone.[1]

Using INS to treat AR improves lung function and reduces airway hyperresponsiveness and exacerbation frequency in people with asthma who are not receiving inhaled corticosteroids.[8]

INS reduce AR symptoms by about 17% more than placebo, but have a variable effect on allergic conjunctivitis.[1] INS are more effective than oral antihistamines or LTRA alone on all aspects of AR. Unlike other treatments, INS reduce nasal congestion.[1]

HCPs should advise patients that the onset of action of INS is 6-8 hours after the first dose. A clinical improvement may not, however, emerge for a few days.[1] The maximal effect may not be apparent for several weeks.[1] Some patients prefer combining an INS plus intranasal antihistamine during the first two weeks of treatment. The antihistamine works more rapidly than the INS.[30]

INS efficacy is broadly similar between different molecules.[1] So, prescribers should consider systemic bioavailability, safety, and ease of device use when choosing the INS.[1] Systemic absorption is negligible with mometasone furoate, fluticasone furoate and fluticasone propionate.[1] In general, therefore, these are the preferred preparations for children and adults. Systemic absorption is modest for most other INS. Betamethasone's high absorption means that this INS should be used short-term only.[1] The BSACI guidelines recommend using INS the "head upside down" position to improve delivery throughout the nasal passages.[1]

INS are generally well tolerated. About 10% of patients experience local nasal irritation, sore throat and/or epistaxis. HCPs should be aware of the risk of hypothalamic-pituitary axis suppression may occur in patients who receive topical corticosteroids for multiple sites (such as use in eczema, asthma and hay fever). In these patients, HCPs should use low bioavailability INS where possible. In addition, HCPs should limit INS use in people predisposed to ocular hypertension and glaucoma.[1]

Several INS contain the preservative benzalkonium chloride, which may irritate the nose, but does not adversely affect mucociliary clearance. Patients who report burning and other symptoms of nasal irritation may benefit from a trial of a benzalkonium-free preparation.[1] HCPs should ensure that patients use the device correctly to limit local adverse effects such as nasal crusting, bleeding and pain.[1]

In people with seasonal AR, a combination spray containing azelastine and fluticasone propionate produces greater symptomatic improvement (including ocular symptoms) than either agent alone. The improvement also emerges more rapidly compared with either agent alone. A small number of patients report a bitter taste.[1]

HCPs need to identify the cause of the nasal obstruction (eg excluding tumours and polyps) before prescribing steroids. INS are the first-line treatment, perhaps combined with a short-term nasal decongestant, for severe nasal obstruction.[1] Steroid drops or oral steroids should be used initially for people with severe nasal obstruction,[1] although because steroids alleviate symptoms they may delay diagnosis of a tumour. An ophthalmologist should supervise the use of topical ocular steroids may be indicated, for example, in people with vernal conjunctivitis.[1]

Intranasal decongestants

Intranasal decongestants cause vasoconstriction, which relieves severe nasal congestion within minutes. The improvement is faster and more marked than with INS. Intranasal decongestants can address eustachian tube dysfunction when flying and increase nasal patency before douching or INS administration allowing delivery beyond the inferior turbinates.[1]

Intranasal decongestants should be used for the short-term treatment of severe nasal congestion only. The BSACI guidelines recommend using intranasal decongestants for fewer than 10 days to reduce the risk that rebound vasodilatation triggers a paradoxical increase in nasal congestion (rhinitis medicamentosa).[1]

Using intranasal decongestants with an INS reduces the risk of rhinitis medicamentosa. Intranasal decongestants can cause nasal irritation and exacerbate rhinitis.[1] The guidelines do not recommend oral pseudoephedrine, which produces a weak response in nasal obstruction and has numerous side-effects.[1]

Leukotriene receptor antagonists

In general, LTRAs are as effective as loratadine in seasonal AR, but are less effective than INS. In absolute terms LTRAs reduce the mean daily rhinitis symptom scores by 5%, which is significantly more than placebo.[38] The response to LTRAs is, however, less consistent than with antihistamines.[1] Nevertheless, LTRAs may have a place in some asthma patients (especially those with exercise-induced or aspirin-exacerbated symptoms) with seasonal AR.[1,30] In general, LTRAs are well tolerated. Some patients report headache, gastrointestinal symptoms or rashes. LRTAs may be associated with neuropsychiatric manifestations in children, especially adolescents, and cause eosinophilic polyangiitis.[1]

Topical anti-cholinergics

Ipratropium bromide can be used three times daily to reduce

rhinorrhoea, but does not improve other nasal symptoms. Add-on topical anti-cholinergics may be effective when INS and antihistamines fail to adequately control watery rhinorrhoea. Topical anti-cholinergics can cause dry nose and epistaxis. While systemic anti-cholinergic effects are unusual, the BSACI guidelines recommend caution in elderly patients.[1]

Biologics

Dupilumab, a monoclonal antibody against IL-4Ra, is approved for severe asthma with type 2 inflammation and CRSwNP. Omalizumab, an antibody targeting IgE is approved for asthma mediated by this immunoglobulin and CRSwNP. Benralizumab and mepolizumab, which block IL-5, are indicated for severe refractory eosinophilic asthma. Biologics are currently prescribed in secondary care, have very specific criteria for initiation and monitoring, and are expensive.

Immunotherapy

Immunotherapy is the only treatment that can modify the course of AR and induce long-term remission. In addition, allergen immunotherapy can alleviate symptoms, reduce medication requirements and improve QoL.[1] There are two approaches: subcutaneous injection immunotherapy (SCIT) and sublingual Immunotherapy (SLIT). The choice depends on patient preference; there are no adequately powered head-to-head trials.[1]

Subcutaneous injection immunotherapy

SCIT is effective for seasonal rhinitis due to pollens and perennial rhinitis due to house dust mite and, although the evidence is less extensive, cat allergens.[1] Pre-seasonal SCIT is effective for pollen allergy.[1] SCIT requires weekly treatment with increasing doses followed by 4-6 weekly maintenance injections for 3-5 years. Because of the risk of anaphylaxis, SCIT should be given only in specialist clinics by trained personnel with immediate access to adrenaline and resuscitation facilities.[1] SCIT is a relatively expensive option.

Sublingual Immunotherapy

SLIT is effective and safe for treatment of AR with and without seasonal asthma caused by grass pollen, ragweed and house dust mite.[1] In children with seasonal AR, SLIT reduces progression to asthma and prevents the development of new allergen sensitisation.[1] A physician supervises the first dose followed by a one-hour observation. SLIT is then administered daily at home.[1] SLIT is well tolerated. The most common side-effects are local itching and mouth and throat swelling.[1] Oral antihistamines before starting SLIT and for the first two weeks can reduce local oral irritation.[1]

Case reports suggest that SLIT may cause systemic reactions and eosinophilic oesophagitis, but no deaths have been reported.[1] A recent Cochrane review concluded that "SLIT may be a safe option for people with well-controlled mild-to-moderate asthma and rhinitis who are likely to be at low risk of serious harm".[39] The limited evidence, however, regarding exacerbations and quality of life meant the authors could not "draw clinically useful conclusions" regarding SLIT's efficacy of SLIT for people with asthma. SLIT's role for people with uncontrolled asthma requires further evaluation.[39]

Improving adherence

Real-world evidence suggests that patients with well-controlled symptoms do not take a medication or use a single treatment. Patients often co-medicate, when they experience uncontrolled symptoms.[5] As this suggests, adherence may be poor. But few real-world studies assessed adherence to AR treatments other than specific immunotherapy.[1]

Estimates of adherence to SCIT, which is injected by a HCP, ranges from 33% to 89%. The time needed (eg having to remain in the clinic following the injection to monitor for side effects and travel time) is the usual reason for poor adherence. Initially, adherence to SLIT is higher (44% to 97%). Nevertheless, fewer than 20% of patients progress to the third year of therapy. The frequency of follow-up visits, perception of poor efficacy and cost contribute to poor adherence.[1] Frequent monitoring and enhanced patient education (eg a formal programme supported with written material) seems to improve adherence to SLIT.[1] Similar principles could apply to other treatments.

Pregnancy and breastfeeding

At least 20% of pregnant women experience rhinitis, which can arise at any time during gestation.[1] Several factors probably contribute to pregnancy-related rhinitis including nasal vascular engorgement and placental growth hormone.[1] Despite being common and having a markedly detrimental effect on QoL, especially during the third trimester, pregnancy-related rhinitis may be inadequately treated.[1] Women with pre-existing AR tend to be the more severely affected during pregnancy.[1]

Often, telling the woman that pregnancy-induced rhinitis is self-limiting offers reassurence.[1] Most medications cross the placenta. So, medicines should only be prescribed when the apparent benefit is greater than the risk to the foetus.[1] Clinical studies have not established the safety of INS during in pregnancy.[1] The BSACI guidelines note, however, that beclomethasone, fluticasone propionate and budesonide have good safety records and are widely used in pregnant women with asthma.[1] Of these, fluticasone propionate shows the lower systemic bioavailability when used nasally.[1]

Among the antihistamines, there is considerable clinical

experience with chlorphenamine, loratadine and cetirizine in pregnancy.[1] Chlorphenamine, however, commonly causes drowsiness, which may affect cycling, driving and other skilled tasks.[40] Nasal lavage is safe and effective in pregnant women, reducing the need for antihistamines.[1] The guidelines suggest avoiding decongestants.[1] Patients on immunotherapy may continue if they have already reached the maintenance phase, but HCPs need to consider the risks and benefits in each case. Immunotherapy should neither be started nor the dose increased during pregnancy.[1]

Similar recommendations can be made about treating AR during lactation. Nasal lavage is safe.[1] Antihistamines are excreted in breastmilk and along with INS should only be used when the benefit outweighs the potential harm to the child. Chlorphenamine may cause drowsiness and poor feeding in the baby. Lower levels of loratadine and cetirizine are found in breastmilk than with chlorphenamine.[1] The lowest dose should be used for the shortest duration whatever treatment is chosen.[1]

Children

Treatment of children follows the same principles as adults, including encompassing the 'one airway, one disease' concept. When choosing treatments, HCPs should consider paediatric needs, such as acceptability, practicality both children and parents, and side-effects.[1]

Nasal saline irrigation is effective for AR in children.[1] Anecdotally, nasal saline irrigation is widely used and HCPs can suggest that patients try this approach. A 3-day course of topical decongestants can be helpful in children with significant nasal blockage to aid INS introduction.[1]

HCPs may need to address parental anxiety associated with continuous INS use. When feasible, prescribers should suggest intranasal steroids with low bioavailability, which have a better safety profile at recommended doses.[1] In addition, HCPs should monitor growth in children, especially those who receive steroids by multiple routes.[1] HCPs can consider a short-course of oral steroids (10–15 mg in the morning for 3–7 days) for children with severe, uncontrolled symptoms that significantly affect QoL.[35]

The BSACI guidelines recommend immunotherapy if children do not adequately respond to maximal pharmacotherapy. SCIT or SLIT may be appropriate for children with seasonal pollen induced rhinoconjunctivitis whose symptoms persist despite INS and antihistamines taken regularly and perennial allergic rhinoconjunctivitis in patients with an allergy to house dust mite who respond inadequately to anti-allergic drug.[1] The decision needs to include the potential for disease prevention.[1] Throughout the treatment journey, HCPs should provide children and carers with the relevant information and appropriate training.

Summary and conclusion

AR the most common immunological disease,[1] remains under recognised and poorly managed, with an under-appreciated socioeconomic impact.[1,2] Diagnosing and treating AR can prove challenging.[2] Clinicians need to be vigilant that AR does not mask an underlying serious conditions and seek red flags at each review. Considerable epidemiological, pathophysiological and clinical evidence now suggests that the upper and lower airways are a single functional and morphological unit.[11] Therefore, considering the upper airways in tandem with the lower airways avoids misdiagnosis and undermanagement. The overlap is not total and HCPs need to use their clinical acumen to individualise treatment to the patient.

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