Cough · 1: Chronic cough in adults
A H Morice, J A Kastelik

The investigation and treatment of chronic cough in adults is generally rewarding, provided there is an understanding of its aetiology, particularly when it arises from sites outside the respiratory tract.

Chronic cough is a common diagnostic and therapeutic problem. The exact prevalence has proved difficult to estimate and recurrent cough is reported by 3–40% of the population. The results of questionnaire surveys such as these are clearly influenced by the population studied and the question posed. In a postal and telephone survey of over 11 000 patients from four general practices in south east England, cough was reported every day or on over half of the days of the year by 14% of men and 10% of women. A survey of 18 277 subjects aged 20–48 years from 16 countries worldwide reported nocturnal cough in 30%, productive cough in 10%, and non-productive cough in 10%. In this study the very high prevalence of nocturnal cough arose because a positive response to the question “Have you been woken by an attack of coughing at any time in the last 12 months?” was taken as indicating the symptom. However, since acute cough—by far the commonest symptom for which medical advice is sought—could also lead to a positive response, significant nocturnal cough was probably overestimated in this study. Whatever the failings of individual surveys, chronic cough is clearly a very common symptom which, although associated with considerable morbidity, goes largely unheeded.

Unsurprisingly, cigarette smoking had a dose related influence on the prevalence of productive cough. In clinical practice, however, smokers readily ascribe their cough to tobacco and rarely seek medical advice specifically to combat this. As a consequence, the incidence of smoking related cough presenting as an isolated symptom in secondary care is low. The reasons why patients seek advice regarding chronic cough are not fully understood, but may be related to worry about the cough. Often, cough related morbidity—in terms of sleep disturbance (either of the patient or their relatives), urinary incontinence in women, or syncope—drives the patient to consult. Indeed, chronic cough has been shown to be associated with a marked deterioration in quality of life which returns to normal on successful treatment.

In population surveys, men have reported cough more frequently. However, most patients referred to specialist cough clinics are women (table 1). This paradox may be explained by differences in smoking habit, but women also appear to have an intrinsically heightened cough response. Inhalation cough challenge is augmented in both healthy female volunteers and female patients with chronic cough. A higher frequency of ACE inhibitor induced cough is also found in women, suggesting that any sex related difference is unlikely to be due to augmented deposition of tussive stimuli in women. A hormonal influence is inferred by the observation that cough reflex sensitivity is similar in boys and girls, but the reason for the marked sex difference in adults remains obscure.

Duration is important in determining the possible aetiology of cough. Classically, cough lasting less than 3 weeks has been considered as acute and that of more than 3 weeks duration has been defined as chronic. In recent years there has been a tendency to redefine chronic cough as cough lasting more than 8 weeks and, for further clarification, the term “subacute cough” was proposed to describe cough lasting 3–8 weeks. While these definitions remain arbitrary, the concept of chronic cough remains clinically important. In this review we will describe the assessment and management of patients with chronic cough.

CLINICAL EXPERIENCE OF CHRONIC COUGH
Chronic cough has frequently been considered to be an intractable problem. Such despondency, however, is not supported by the experience of specialist cough clinics. In these tertiary referral centres, which presumably concentrate on the most difficult diagnostic problems, an accurate diagnosis leading to effective treatment is achieved in over 80% of patients. This contrasts markedly with the experience in non-specialist clinics. The main reason for this difference is a failure to consider the potential origin of cough as being outside the lower respiratory tract. Because cough may arise from anywhere in the distribution of the vagus, the full assessment of the patient with chronic cough relies on a multidisciplinary approach and close cooperation between gastroenterology and ENT departments, as well as respiratory medicine. If this approach is adopted, only a small number of patients with idiopathic cough remain in whom no diagnosis is determined.

SYSTEMATIC ASSESSMENT OF COUGH
Twenty years ago Irwin and colleagues suggested that the investigation of patients with chronic cough could be based on an “anatomical diagnostic protocol” and that, if such an approach was used, “the outcome of specific therapy, almost without exception, is successful and sustained.” Our knowledge of the anatomical

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and cellular basis for cough receptor stimulation has evolved since that time, both in terms of conditions known to cause cough and the mechanisms whereby the cough reflex is stimulated in disease. However, the concept of a logical diagnostic pathway leading to successful specific treatment remains the basis of the organisation of the specialist cough clinic reported in the literature. In the absence of such an approach, the diagnostic yield and outcome of treatment is poor.\(^{22,26}\)

Limited experience from general practice suggests that over 90% of patients with chronic cough, who represented approximately 6% of all new referrals, had their cough attributed to either bronchial hyperresponsiveness or upper airway disease.\(^{25}\) In contrast, a survey from a general respiratory clinic revealed that over half the patients with cough had underlying lung disorders such as chronic obstructive pulmonary disease (COPD), bronchiectasis, pulmonary fibrosis, or lung cancer.\(^{22}\) Thus, when examining the cough mechanisms whereby the cough reflex is stimulated in disease. However, the concept of a logical diagnostic pathway leading to successful specific treatment remains the basis of the organisation of the specialist cough clinic reported in the literature. In the absence of such an approach, the diagnostic yield and outcome of treatment is poor.\(^{22,26}\)

Methodological differences in how a diagnosis is accepted as the cause of cough are also likely to be important. In the study by Palombini et al\(^\text{26}\) patients underwent more than 12 different diagnostic procedures and were considered to be positive for a diagnosis if a test result was abnormal. Unsurprisingly, this approach led to the claim that multiple causes of cough could be identified in over 60% of patients. Even when the investigation is tailored to the presenting symptoms, multiple diagnoses are made. For example, Irwin et al\(^\text{27}\) reported multiple aetiology for cough in a quarter of his patients. The more conservative approach of determining diagnosis, adopted particularly in European centres, has shown that in 89–100% of patients a single cause of chronic cough can be established.\(^{22,28-30}\) However, a concomitant increase has been observed in the number of patients with idiopathic cough. Whereas Irwin et al\(^\text{27}\) and Palombini et al\(^\text{26}\) came to a diagnosis in all but one of 249 unselected patients, firstly Poe et al\(^\text{11}\) and subsequently several other groups\(^{28,12}\) have failed to achieve such diagnostic excellence, even when the anatomical diagnostic protocol was rigorously followed.

O’Connell et al\(^\text{10}\) were the first to suggest that a different approach based on the empirical treatment of cough could lead to an improved diagnostic yield. In this study patients were allotted treatment when intensive investigations had failed to provide a diagnosis. The finding that a number of patients did not achieve a primary diagnosis is perhaps unsurprising in the knowledge that more recent studies have described previously unrecognised causes of chronic cough such as eosinophilic bronchitis,\(^{37}\) eosinophilic tracheobronchitis,\(^{38}\) and oesophageal dysmotility.\(^{39-41}\) The plan of investigation used at that time would not have been capable of picking up these newly discovered associations and it is likely that those patients currently classed as having idiopathic cough will have as yet undiscovered syndromes.

Several investigators have attempted to enhance diagnosis with the evaluation of upper airway inflammation,\(^{37}\) the analysis of induced sputum for cytokines, interleukins or TNF-alpha,\(^{42}\) and the measurements of exhaled nitric oxide levels.\(^{43}\) These efforts have, however, met with limited success. Conversely, it is possible that a simplified approach with a therapeutic trial as the main diagnostic arm of a cough clinic protocol may be successful. This strategy could be used earlier to provide a diagnosis without the need for specialised investigations. The approach of symptom led therapeutic trials requires a thorough knowledge of the likely aetiology and incidence of the various cough syndromes.

### Chronic cough syndromes

There are three common causes of chronic cough: asthma, oesophageal disease, and rhinitis. This “diagnostic triad”\(^\text{\textsuperscript{26}}\) contains the overwhelming majority of patients who suffer from chronic cough.

#### Asthma related syndromes

The diagnosis of asthma as provided in the UK guidelines relies on the evidence of variability of airflow obstruction, either spontaneous or pharmacologically induced.\(^{40,41}\) However, the US National Institutes of Health definition\(^\text{\textsuperscript{42}}\) states that asthma is “a clinical syndrome characterised by increased responsiveness of the tracheobronchial tree to a variety of stimuli”. This latter definition allows for asthma without airflow obstruction such as that which occurs in cough variant or, more accurately, cough predominant asthma. Our concentration on measures of variable airflow obstruction in the diagnosis of adult asthma has been led by practice in clinical trial design.\(^{43}\) Here reversibility to salbutamol or diurnal variation in peak expiratory flow are almost universally used as entry criteria to establish the diagnosis. Reversibility to β agonists is very good for proving that patients have asthma but is not reflected in the generality of asthma patients. Indeed, less than 10% of an asthmatic population may exhibit spirometric reversibility.
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The chronic cough in adults is reliably a syndrome with such protean manifestations. This problem has been extensively discussed and it is clear that no single test has sufficient sensitivity and specificity to diagnose reliably a syndrome with such protean manifestations. This is particularly relevant when cough is the primary presenting complaint. The term “variant asthma” or “cough variant asthma” to describe asthma associated with cough was originally introduced by Glauser. This entity was more clearly defined in 1979 by Corrao and colleagues who described six patients with chronic cough, bronchial hyperresponsiveness, and a response to anti-asthma medication but without wheezing and airflow obstruction. Subsequently, the term “cough predominant asthma” was proposed by Pratter and colleagues based on the suggestion that cough is not a separate entity but part of the spectrum of asthma together with dyspnoea and airflow obstruction. In our experience, this term more accurately describes the patients seen in clinical practice.

Niimi et al. demonstrated the presence of eosinophilic inflammation in cough predominant asthma and a further variant, eosinophilic bronchitis, characterised by airway eosinophilia but without bronchial hyperresponsiveness. Originally described by Gibson and colleagues, eosinophilic bronchitis may be detected in patients with chronic cough where reliable sputum induction and analysis is available. Whether cough with sputum eosinophilia but without airflow reversibility or hyperresponsiveness is a form of asthma remains debatable. The different facets of the syndrome may be due to the differential location of inflammatory cells, particularly mast cells, within the airway. However the terms “eosinophilic bronchitis” and “cough predominant asthma” appear to be clinically useful (table 2).

All of these facets of the “cough/asthma syndrome” usually improve with inhaled corticosteroids. The early symptomatic response to inhaled corticosteroids in “classical asthma” may be delayed in chronic asthmatic cough. Similarly, in eosinophilic bronchitis significant improvements in cough threshold and sputum eosinophilia have been observed after 4 weeks of treatment with budesonide. However, treatment may be required for several months before maximum improvement is observed. In this regard, cough may be similar to the slow improvement in airway hyperresponsiveness seen with inhaled corticosteroids in “classical asthma”. This phenomenon of a delayed response is also true of treatment for the other cough syndromes. Patients with possible asthmatic cough presenting to secondary care (in the UK) are almost invariably on inhaled corticosteroids, and a poor response may indicate the usual problems with asthma therapy. Everard’s “three Cs” of competence, contrivance and compliance should be applied. An initial trial of prednisolone may be helpful. Since bronchoconstriction is not usually a major feature, an alternative diagnostic strategy is to stop inhaled corticosteroids. A progressive worsening of cough, with or without deterioration in peak expiratory flow, confirms the diagnosis.

This also allows sputum examination since even moderate doses of inhaled corticosteroids cause a dramatic fall in the sputum eosinophil count. The subsequent symptomatic improvement on reinstitution of treatment reinforces the diagnosis and is associated with an improvement in cough sensitivity (fig 1).

In patients who remain symptomatic on moderate doses of inhaled corticosteroids there is no clear evidence based strategy. Two recent studies reported on the effects of leukotriene receptor antagonists on the cough reflex. While zafirlukast had no effect on the normal cough response in classic asthma, it showed marked antitussive effects in patients with cough predominant asthma. The fact that lipoxigenase products have been shown to have a major modulatory role on the putative VR1 cough receptor may indicate a specific role for these agents in asthmatic cough. Fujimura et al. have also described a response to antihistamines in a syndrome they termed eosinophilic tracheobronchitis or “atopic cough”.

As in all the conditions illustrated in table 2 cough improves with corticosteroids, the term “corticosteroid responsive cough” as used by Gibson and colleagues in the original paper describing eosinophilic bronchitis may provide a convenient simplification. However, it is important to realise that non-asthmatic cough could be steroid responsive, both in rhinitis and in gastro-oesophageal reflux. An increased eosinophil count can be seen in the bronchoalveolar lavage fluid of patients with GOR related cough and airway inflammation is unsurprisingly seen in patients with reflux. This latter may be confirmed on direct examination of the endolarynx (fig 2). Thus, in patients with laryngopharyngeal reflux, erythema or, more commonly, oedema of the arytenoid, interarytenoid area, and laryngeal surface of the epiglottis is present, together with oedema of the vocal cords and Reinke’s space (lamina propria of the true vocal cords). These changes may lead to a characteristic obliteration of the ventricle, the groove between the true and false vocal cords.

### Table 2 Corticosteroid responsive cough syndromes

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>PEF variability</th>
<th>Bronchial hyperresponsiveness</th>
<th>Sputum eosinophilia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classical asthma</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Cough variant of asthma</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Eosinophilic bronchitis</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

![Figure 1](image-url) Improvement in cough reflex sensitivity measured by citric acid cough challenge in response to inhaled corticosteroids in a patient with cough variant asthma.
event—that is, occurring simultaneously with or shortly after a fall in pH—should be measured. 69 71 83 In an elegant experiment Ing et al 70 demonstrated this effect by infusion of acid into the lower oesophagus. In a proportion of patients, however, cough can also be induced by intra-oesophageal infusion of 0.9% saline. 69 70 This supports the hypothesis that cough may be induced not only by acidification, but also by other stimuli. Abnormal oesophageal manometry such as low gastro-oesophageal sphincter pressure leading to volume reflux and disordered oesophageal peristalsis also contribute in patients with chronic cough. 32 36 It is possible that the role of non-acid reflux may be further clarified by measuring oesophageal impedance. 64 85

Chronic cough associated with gastro-oesophageal disorders frequently improves with antireflux therapy. 69 71 Conservative measures such as weight reduction, high protein low fat diet, elevation of the head of the bed, and lifestyle modification including avoidance of caffeine, smoking, and chocolate are often recommended, although the basis for this advice is unclear. H2 antagonists, 23 27 71 proton pump inhibitors, 30 32 76 and prokinetic medication 23 27 86 have been used, but proton pump inhibitors—particularly at high doses—seem superior in treating cough. 69 70 In patients with abnormal oesophageal manometry but normal 24 hour pH monitoring, proton pump inhibitors also appear effective. 71

The three placebo controlled trials reported to date have confirmed that both H2 antagonists and proton pump inhibitors correct chronic cough in patients with gastro-oesophageal reflux. 73 77 78 These studies reported a relatively slow response in cough, ranging from 8 to 12 weeks. Occasionally, however, 6 months or longer may be required for the cough to improve. 23 27 Unfortunately, antireflux agents do not fully suppress acid secretion and do not alter the frequency of reflux events. 82 87 Antireflux surgery such as fundoplication may be successful in the face of an inadequate medical response. 83 86 However, the role of surgery has yet to be fully evaluated.

**Rhinitis, sinusitis, and postnasal drip**

In contrast to the relative precision with which the asthma syndromes and oesophageal cough can be investigated, the association of chronic cough with upper airway disease frequently lacks objective verification. Many series, mainly from the US literature, report that postnasal drip syndrome (PNDS) is one of the most common causes of chronic cough. 30 32 49 86 However, this term describes a symptom complex that does not have any objective or pathognomonic findings. 20 The diagnosis of PNDS rests on eliciting symptoms that include the sensation of “something dripping into the throat”, frequent throat clearing, nasal congestion or discharge. 23 27 Such symptoms are common in non-coughing individuals and vary enormously in different societies. A large telephone survey of cold symptomatology found that over 50% of subjects contacted in the USA associated a cold with PNDS, whereas less than a quarter in the UK and virtually no respondents from Latin America and India admitted to the symptom (Dr Hull, Procter & Gamble, personal communication).

Rhinitis is a much simpler term describing the location of airway inflammation. Sinusitis is present clinically when there is facial pain and may be associated with mucosal thickening, opacification of a sinus or an air-fluid level, and response to antibiotics. 30 36 Sinus imaging has been suggested to support the diagnosis. 33 17 86 However, in the context of chronic cough, sinus imaging appears to be unhelpful and of low predictive value. 12 89

The common use of the term PNDS in cough has been led by clinicians who have observed that combinations of antihistamines and decongestants are effective in treating...
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some patients with chronic cough.23 27 Pratter et al.40 49 using a stepped approach that involved the initial treatment of all patients with chronic cough with antihistamine decongestants, diagnosed PNDS in over 80% of cases. Some of these patients were asymptomatic apart from cough and they proposed the term “silent” postnasal drip syndrome since cough was the sole manifestation of PNDS. Obviously there are many more explanations for this therapeutic success than PNDS. However, these observations underscore the importance of histamine in chronic cough, either through a central activity or possibly due to its role in airway inflammation.41

A key question in cough associated with rhinitis is how the afferent sensory input generating the cough is developed. In animal studies no cough sensitive innervation can be seen above the larynx.50 Recently, based on the observation of a high frequency of asthma coexisting with allergic rhinitis, Grossman93 introduced a concept of “one airway, one disease”. Thus, upper and lower airway diseases are described as a continuum of inflammation involving one airway that may have a common origin for the underlying pathological process. In cough the coexistence of asthma and rhinitis has been reported for many years.23 27 94 Whether upper airway disease contributes to cough via PNDS or is merely a marker remains uncertain.95 Some support for the “one airway, one disease” concept in the pathophysiology of cough was provided by the response to histamine H1 antagonists and corticosteroids in patients with “atopic cough”.96 97 Better clarification of the description of rhinitis associated cough based on a scheme such as the ARIA guidelines98 needs to be developed.

OTHER CAUSES OF CHRONIC COUGH

Many other conditions can give rise to chronic cough. Typically, cough is the major component of a well recognised clinical syndrome such as chronic bronchitis, pulmonary fibrosis, or bronchiectasis. There are, however, a number of causes of cough which still provide diagnostic confusion.

ACE inhibitor cough

That a systemically active drug could cause cough as a side effect went unrecognised for many years.65 67 Cough associated with angiotensin converting enzyme (ACE) inhibition occurs in up to 15% of patients and has a very variable onset and offset.66 67 Because ACE inhibitors appear to alter the sensitivity of the cough reflex,68 underlying subclinical cough such as that from reflux may now declare itself. Cessation of treatment with ACE inhibitors returns the cough reflex to normal,69 70 but the plasticity of the reflex varies and it may take several months for the cough to settle in some individuals.101 Several small scale studies have reported a beneficial effect from a variety of agents in ACE inhibitor induced cough.102-104 None have proved useful in clinical practice. The alteration in the sensitivity of the cough reflex precludes the full assessment of patients with cough while the patient remains on treatment. Indeed, alternative agents such as angiotensin II antagonists provide the beneficial effects of ACE inhibition without the tendency to cough.105

Occupational exposure

Cough may be an important symptom in a number of occupational lung diseases, particularly asthma. Cough as an isolated finding may occur following chronic exposure to low molecular weight irritants. In a glass bottle factory workers exposed to hydrochloric acid and organic oils developed chronic cough without airways hypersensitivity to methacholine. Cough reflex hypersensitivity was demonstrated by inhalation challenge with capsaicin and citric acid.106 107

Post infectious cough

Occasionally, patients give a striking history of prolonged cough following a relatively minor respiratory tract infection. If recurrent, then anatomical lesions such as bronchiectasis need to be excluded. Some agents such as Bordetella species are notorious for causing prolonged cough and recent studies have suggested that, in adults, infection and repeat infection are relatively common.108 109

Systemic illness

A number of systemic disorders, either organ specific autoimmune diseases110 or vasculitic disorders,111 may present with cough. These illustrate the non-specific nature of cough as a response to airway inflammation.

CONCLUSION

The investigation and treatment of chronic cough is a rewarding and generally fruitful undertaking. By adopting an approach based on a careful history, simple investigations and therapeutic trials, dramatic improvements in quality of life can be achieved at little cost. The main reason for failure is a lack of understanding of the aetiology of cough, particularly when it arises from sites outside the respiratory tract.

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REFERENCES


5 Schappert KT. National Ambulatory Medical Care Survey: 1991 summary Advance Date, 1993


11 Lambert PM, Reid DD. Smoking, air pollution, and bronchiectasis in Britain. Lancet 1970; i: 853-7


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Eosinophilic bronchitis is an important cause of chronic cough. 

To identify patients who have eosinophilic bronchitis, airway inflammation was assessed in 140 patients, the majority of whom were symptomatic. The following criteria were fulfilled: a history of chronic cough with at least two of the following symptoms: 

1. Worsening of symptoms with exercise or upper respiratory tract infections.
2. Symptom duration of at least 3 months.
3. Symptom improvement with inhaled corticosteroids.
4. Symptom improvement with systemic corticosteroids.
5. Symptom improvement with midodrine.
6. Symptom improvement with tiotropium bromide.

The diagnosis of eosinophilic bronchitis was made if at least three of the above criteria were present for at least 6 months. The diagnosis was confirmed by the presence of at least 20 eosinophils per high-power field on bronchoalveolar lavage fluid or biopsy specimens.

Asthma is a chronic inflammatory disease of the airways that causes variable airflow obstruction. The inflammation is mediated by multiple inflammatory cells and cytokines, but its pathogenesis remains poorly understood. 

In the United Kingdom, asthma is the most common chronic disease in children and adults, affecting approximately 9 million people. 

The prevalence of asthma is increasing worldwide, and the economic burden is substantial. 

Asthma is characterized by airway hyperreactivity, which is defined as an increased responsiveness of the airways to a variety of stimuli. 

Airway hyperreactivity can be assessed using a variety of methods, including peak expiratory flow (PEF) monitoring, bronchial challenge tests, and fraction of inspired oxygen (FiO2) measurements. 

Bronchial challenge tests are used to assess airway reactivity and are performed by administering increasing doses of a bronchoconstrictor, such as methacholine, to a subject while measuring the PEF. 

In addition to airway hyperreactivity, asthma is characterized by airway inflammation, which is thought to play a role in the development and maintenance of the disease. 

Airway inflammation can be assessed using various methods, including bronchoalveolar lavage (BAL), bronchial biopsy, and endobronchial ultrasound (EBUS). 

BAL is a minimally invasive technique that allows the collection of cells and fluids from the airways. 

Bronchial biopsy is a more invasive technique that involves the removal of tissue from the airways for histological examination. 

EBUS is a technique that uses real-time ultrasound to visualize structures within the airway lumen. 

The presence of inflammatory cells, such as eosinophils, neutrophils, and lymphocytes, is indicative of airway inflammation. 

Eosinophils are a type of white blood cell that play a central role in the pathogenesis of asthma. 

Eosinophils are recruited to the airways in response to allergens and other inflammatory stimuli. 

Eosinophilic inflammation is characterized by the accumulation of eosinophils in the airways, which can lead to airway hyperreactivity and bronchial obstruction. 

Eosinophilic inflammation is associated with increased levels of specific biomarkers, such as eosinophil cationic protein (ECP), eosinophil-derived neurotoxin (EDN), and eosinophil major basic protein (EMBP). 

Eosinophils are thought to play a role in the development and maintenance of asthma by releasing pro-inflammatory mediators, such as leukotrienes, cytokines, and chemokines. 

Leukotrienes are a family of lipids that are involved in the regulation of airway smooth muscle tone, vascular permeability, and edema. 

Cytokines are signaling molecules that are involved in the regulation of immune responses. 

Chemokines are a type of cytokine that are involved in the recruitment and activation of inflammatory cells. 

Eosinophils release chemokines, such as CCL20, which can attract other eosinophils and neutrophils to the airways. 

Eosinophils also release cytokines, such as IL-13, which can promote the survival and differentiation of eosinophils. 

In addition to eosinophils, neutrophils are another type of inflammatory cell that are commonly found in the airways of patients with asthma. 

Neutrophils are recruited to the airways in response to inflammatory stimuli and play a role in the resolution of acute airway inflammation. 

Neutrophils release pro-inflammatory mediators, such as neutrophil elastase, which can contribute to airway hyperreactivity. 

Neutrophils also play a role in the recruitment of other inflammatory cells, such as eosinophils, to the airways. 

Lymphocytes are another type of white blood cell that play a role in the immune response. 

T lymphocytes, in particular, are thought to play a role in the development and maintenance of asthma by releasing pro-inflammatory cytokines, such as IL-4 and IL-13. 

B lymphocytes are involved in the production of antibodies, which can play a role in the pathogenesis of asthma. 

The role of B lymphocytes in asthma is not well understood, but they are thought to play a role in the regulation of immune responses. 

The relationship between inflammatory cells and markers of airway inflammation is complex and is still being studied. 

Future research is needed to better understand the role of inflammatory cells in the pathogenesis of asthma and to develop new therapeutic targets for the treatment of the disease.
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Thorax 2003 58: 901-907
doi: 10.1136/thorax.58.10.901

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