definite esophagitis by endoscopy, have been restricted because many patients with extraesophageal manifestations of reflux may not have esophagitis. The development of reliable and practical techniques for ambulatory prolonged recording of intraesophageal pH has allowed more precise identification of the potential relationship between abnormal amounts of GE reflux and these clinical syndromes. Studies of this kind have revealed that many patients with chronic hoarseness or intermittent bronchospasm will have abnormal reflux patterns, often in the absence of esophagitis.

One has to be somewhat cautious, however, in accepting excessive acid exposure in the distal esophagus as proof of causation for these extraesophageal manifestations. In the case of bronchospastic symptoms, this dilemma is compounded by the knowledge that bronchodilating drugs, such as theophylline, can produce decreases in lower esophageal sphincter pressure. Thus, the abnormal reflux in these patients could be a result of the patient's therapy, rather than a cause of the patient's symptoms.

With these reservations, in our large experience with 24-hour pH monitoring, we have come to regard both chronic hoarseness and intermittent bronchospasm as indications for using this diagnostic test. In the case of asthma, we feel that the test becomes a greater diagnostic aid if the patient's intermittent symptoms can be shown to be regularly associated with a decrease in the intraesophageal pH to less than 4.0 during testing. This is particularly helpful if nocturnal wheezing is shown to occur in direct association with a reflux episode monitored during sleep. More recently, there have been attempts to apply a "double probe" pH recording technique to identify high reflux by placing a second probe in the upper esophagus or just above the upper esophageal sphincter. To date, these studies have been only somewhat helpful, with only occasional patients shown to have clear acid exposure in these more proximal locations. Some of this may be due to the difficulty of proper placement of the second probe to recognize the minute amounts of acid which might trigger bronchospasm. This concept is further compounded by the suggestion that there are potentially two mechanisms by which GE reflux might produce bronchospasm, either by direct aspiration of small amounts of acid or by a reflex occurring secondary to distal esophageal acid exposure. Thus, it is not essential that high reflux be identified or even be responsible, in reflux-related asthma. There have been some attempts to document actual aspiration of gastric contents in patients with unexplained chronic pulmonary symptomatology. By the use of radioisotopic tagging of gastric contents, aspiration may conceivably be documented during subsequent scanning of the chest. These studies have often been done with 99mTc because the absorbed isotope is secreted by the gastric parietal cell, thus providing a constant source of isotope tag in the gastric secretions. Unfortunately, the isotope is also secreted by the salivary glands, raising the question whether aspirate containing the isotope truly represents gastric contents. Hopefully, in the future we will identify even better techniques for monitoring acid exposure in the hypopharynx or identifying the patient with mini-aspiration of gastric contents.

The manuscript by Perrin-Fayolle provides valuable insights into the clinical syndrome of reflux bronchospasm. One would hope that it will stimulate a greater clinical awareness of this problem, trials of antireflux medical therapy in patients of this kind, and further clinical investigation to help clarify diagnosis and therapy in these patients. For the present, these investigators have helped us recognize that we should be particularly suspicious of the potential for GE reflux as an etiologic factor in the patient with intrinsic asthma with recurring nocturnal bronchospasm and/or tracheitis, particularly if symptoms of heartburn and regurgitation have preceded the development of asthma.

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Bronchocentric Granulomatosis
Disease or Diagnosis?

Lebow coined the expression "bronchocentric granulomatosis" in 1973 to describe one of five pulmonary angitis and granulomatosis syndromes. He
defined the lesion in purely pathologic terms as necrotizing granulomatous inflammation centered upon peripheral conducting airways. Bronchocentric granulomatosis has since emerged as a relatively nonspecific pathologic response to various forms of airway injury.

Approximately one-third to one-half of reported examples of bronchocentric granulomatosis have been associated with allergic bronchopulmonary aspergillosis (ABPA).3-5 ABPA is a syndrome that mainly affects asthmatic patients and consists of fleeting pulmonary opacities, eosinophilia, elevation of serum IgE, and evidence of Aspergillus hypersensitivity. The diagnosis is usually made clinically, and most patients respond to corticosteroid therapy. In this condition, bronchocentric granulomatosis is part of a complex tissue response to airway colonization by fungal organisms.2,4 There are usually other associated tissue manifestations of hypersensitivity including mucoid impaction of bronchi, eosinophilic bronchiolitis, and eosinophilic pneumonia. Fungal hyphae can be identified in most of these cases and are located within the bronchocentric granulomas as well as the impacted mucus.2,4

Bronchocentric granulomatosis has been reported more commonly in nonasthmatic subjects who lack evidence of fungal hypersensitivity. These patients comprise a heterogeneous group in whom the pathogenesis of the granulomatous inflammation is usually unknown.2,3,5 They differ from asthmatic patients in that respiratory complaints are more often mild, peripheral eosinophilia is uncommon, and other tissue manifestations of ABPA are lacking. Most patients in this group have recovered with no specific therapy or surgical excision.2,3,5 Corticosteroids have been used in some cases. Bronchocentric granulomas can occur in other conditions, including rheumatoid arthritis, Wegener's granulomatosis, and pulmonary echinococcosis. Certain pulmonary infections, including blastomycosis, histoplasmosis, tuberculosis, and atypical mycobacteria can also cause granulomatous destruction of bronchioles similar to that seen in bronchocentric granulomatosis.6,7 Recognition of these patients is important because specific antimicrobial therapy is the treatment of choice.

In this issue of Chest (see page 92), Tazelaar and colleagues describe bronchocentric granulomatosis as a manifestation of fungal infection after heart-lung and allogeneic bone marrow transplantation. Although certain chronic airway diseases are well recognized complications in long-term survivors of both procedures, this is the first report of bronchocentric granulomatosis in this group of patients. No associated changes of allergic bronchopulmonary diseases were present in any of their patients. Aspergillus sp were identified within the granulomas in both heart-lung transplant recipients, and Mucor was present in the bone marrow transplant patient. Two patients died with disseminated infection despite the absence of identifiable tissue invasion, and the third was improving with amphotericin B therapy.

The report by Tazelaar et al emphasizes that bronchocentric granulomatosis is not a disease, but rather a descriptive pathologic diagnosis. The authors attempt to avoid the confusion by introducing a morphologically accurate designation, bronchocentric mycosis, to describe the findings in their patients. We would do well to follow their example and restrict the term bronchocentric granulomatosis to: 1) asthmatic patients, in whom this lesion should be considered a manifestation of ABPA, and 2) nonasthmatic subjects in whom other causes of granulomatous inflammation have been vigorously excluded. The significance of the diagnosis in this latter group is uncertain, however, and it should not be construed as a specific clinicopathologic entity. Etiologically precise terms should be used for all other patients in whom an underlying cause is established (eg, histoplasmosis, blastomycosis, tuberculosis, echinococcosis, Wegener's granulomatosis). Finally, the term bronchocentric granulomatosis should be avoided in immunocompromised hosts. When necrotizing granulomas are present within lung tissue in this group of patients, invasive infection should be the primary consideration regardless of the microscopic distribution of the lesions.

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