

## Obliterative bronchiolitis, cryptogenic organising pneumonitis and bronchiolitis obliterans organizing pneumonia: three names for two different conditions

R.M. du Bois, D.M. Geddes

Over the last five years, increasing confusion has developed over the use of the terms "bronchiolitis obliterans" and "bronchiolitis obliterans organizing pneumonia". The confusion stems largely from the common use of the term "bronchiolitis obliterans" or "obliterative bronchiolitis" in the diagnostic labels applied to two entities which are quite distinct clinically but which bear certain resemblances histologically.

### Obliterative bronchiolitis

In 1977, GEDDES *et al.* [1] reported the case histories of six patients whose clinical condition was characterized by airways obliteration in association with rheumatoid arthritis. The striking clinical features were of rapidly progressive breathlessness and the finding on examination of a high-pitched mid-inspiratory squeak heard over the lung fields. Chest radiographs showed hyperinflated lungs but were otherwise normal. Lung function studies revealed a predominantly obstructive ventilatory defect with normal gas transfer coefficient. The central feature of the pathological appearances of the lungs at autopsy examination was a narrowing or obliteration of the majority of airways measuring 1-6 mm in diameter but the alveolar ducts and alveoli were spared.

Three of the six patients described in this series, had received d-penicillamine. Subsequent studies have described patients with rheumatoid arthritis and obliterative bronchiolitis with no history of d-penicillamine ingestion, and obliterative bronchiolitis is not described in other conditions for which d-penicillamine has been prescribed. It is concluded, therefore, that the entity is associated with rheumatoid arthritis.

Other reports have described a similar clinical syndrome in association with graft *versus* host disease in bone marrow transplantation [2], rejection in lung transplantation [3], the response to viral infection [4], the response to the ingestion of certain drugs other than d-penicillamine [5], and in a group of patients in whom no initiating factor could be identified [6]. In all of these syndromes, the label obliterative bronchiolitis

has been applied to conditions in which airflow obstruction is prominent and in which response to treatment is poor.

### "Cryptogenic organizing pneumonitis" or "bronchiolitis obliterans organizing pneumonia" (BOOP)

Cryptogenic organizing pneumonitis was first described by DAVISON *et al.* [7] in 1983. The clinical syndrome consisted of breathlessness, malaise, fever, high erythrocyte sedimentation rate (ESR), pneumonic shadowing on chest radiograph with a restrictive pulmonary function defect and low gas transfer coefficient. On histological examination of lung biopsy material, the typical and distinguishing feature was the presence of connective tissue within the alveoli, alveolar ducts and, occasionally, in respiratory bronchioles. This connective tissue consisted of "loosely woven fibres of collagen and reticulin" but with preservation of the bronchoalveolar architecture. In some patients, interstitial involvement in the form of chronic inflammatory cells and some fibrosis was also present. Cryptogenic organizing pneumonitis was readily corticosteroid responsive and patients rapidly improved on such therapy as measured by symptomatic, chest radiographic and physiological indices.

The nomenclature became clouded in 1985 with the publication of an article by EPLER *et al.* [8] of an entity which they termed "bronchiolitis obliterans organizing pneumonia". They reported a series of patients who were selected on the basis of pathological reports on biopsy material collected over a 30 yr period between 1950 and 1980. The essential selection criterion for inclusion in the study was the mention of the term "bronchiolitis obliterans" in description of open lung biopsies, and this was subsequently correlated with radiographic and physiological features, and response to treatment. This entity, now widely known as BOOP, is identical to cryptogenic organizing pneumonitis. In 57 of this series of 67 patients, plugs of granulation tissue was observed, predominantly in terminal and respiratory bronchioles, alveolar ducts and alveoli. Obliteration of airways by mature fibrous tissue is not described. The remaining ten patients had histological lesions limited to the small airways without parenchymal involvement.

Table 1. - Comparison of obliterative bronchiolitis (OB) and cryptogenic organizing pneumonitis (COP or BOOP)

	Clinical	Physiological	Pathology		Corticosteroid response
			Airways	Alveoli	
OB	Airways obstruction	Obstruction Kco normal	Widespread obliteration of bronchioles	Spared	Poor
COP	Pneumonia	Obstruction uncommon Impaired gas exchange	Involvement of respiratory bronchioles (50%) alveolar ducts (67%)	Organizing pneumonia	Good

Kco: carbon monoxide transfer coefficient; BOOP: bronchiolitis obliterans organizing pneumonia.

Since this report, there have been a number of publications describing the association of various diseases and drug therapies with the finding on pathological evaluation of intra-alveolar connective tissue similar to that described by DAVIDSON *et al.* These include ulcerative colitis [9], primary biliary cirrhosis [10], amiodarone [11], acebutolol [12] and gold therapy [13]. More recently the clinical pattern of cryptogenic organizing pneumonitis and the appropriate histological features have been described in three patients with rheumatoid arthritis in whom the response to corticosteroids was good [14]. DAVIDSON *et al.* there was no association with rheumatoid arthritis but in a report by YOUSEM *et al.* [15], in which 40 open lung biopsies from patients with rheumatoid arthritis were assessed, the presence of intra-alveolar connective tissue deposition was described in six patients although the clinical features of these are not described in detail. In the present issue another case of BOOP in a patient with rheumatoid arthritis is presented [16]. BOOP must, therefore, also be included in the spectrum of pulmonary disorders which may be found in association with rheumatoid arthritis.

There are a number of good reasons for making a clear distinction between obliterative bronchiolitis and BOOP as indicated in table 1.

Since the small airways are often involved in a wide range of diseases, such as chronic bronchitis and extrinsic allergic alveolitis (hypersensitivity pneumonitis), a condition in which buds of intra-airway organizing connective tissue are also seen, we believe that the use of a pathological descriptive term to define a clinical condition has caused confusion. We suggest that these two quite distinct clinical entities are called obliterative bronchiolitis and cryptogenic organizing pneumonitis.

#### References

- Geddes DM, Corrin B, Brewerton DA, Davies RJ, Turner-Warwick M. - Progressive airway obliteration in adults and its association with rheumatoid disease. *Q J Med*, 1977, 184, 427-444.
- Wyatt SE, Nunn P, Hows JM, Yin JAL, Hages MC, Catovsky D, Gordon-Smith EC, Hughes JMB, Goldman JM, Galton DAG. - Airways obstruction associated with graft versus host disease after bone marrow transplantation. *Thorax*, 1984, 39, 887-894.
- Burke CM, Theodore J, Dawkins KD, Yousem SA, Blank N, Billingham ME, van Kessel A, Jamieson SW, Dyer PE, Baldwin JC, Stinson EB, Shumway NE, Robin ED. - Post-transplant obliterative bronchiolitis and other late sequelae in human heart-lung transplantation. *Chest*, 1984, 86, 824-829.
- Ham JC. - Acute infectious obstructing bronchiolitis. A potentially fatal disease in the adult. *Ann Intern Med*, 1964, 60, 47-60.
- Cooper JAD, White DA, Matthay RA. - Drug-induced pulmonary disease. Part 2. Noncytotoxic drugs. *Am Rev Respir Dis*, 1986, 133, 488-505.
- Turton CW, Williams G, Green M. - Cryptogenic obliterative bronchiolitis in adults. *Thorax*, 1981, 36, 805-810.
- Davidson AG, Heard BE, McAllister WAC, Turner-Warwick MEH. - Cryptogenic organising pneumonitis. *Q J Med*, 1983, 207, 382-494.
- Epler GR, Colby TV, McLoud TC, Carrington CB, Gaensler EA. - Bronchiolitis obliterans organising pneumonia. *N Engl J Med*, 1985, 312, 152-158.
- Swinburn CR, Jackson GJ, Cobden I, Ashcroft T, Morrill GN, Corris PA. - Bronchiolitis obliterans organising pneumonia in a patients with ulcerative colitis. *Thorax*, 1988, 43, 735-736.
- Davidson AG, Epstein O. - Relapsing organising pneumonitis in a man with primary biliary cirrhosis, CREST syndrome, and chronic pancreatitis. *Thorax*, 1983, 38, 316-317.
- Kennedy JI Jr. - Clinical aspects of amiodarone pulmonary toxicity. *Clin Chest Med*, 1990, 11, 119-129.
- Camus P, Lombard J-N, Perrichon M, Piard F, Guerin J-C, Thivolet FB, Jeannin L. - Bronchiolitis obliterans organising pneumonia in patients taking acebutolol or amiodarone. *Thorax*, 1989, 44, 711-715.
- McCormick J, Cole S, Lahiri B, Knauff F, Cohen S, Yoshida T. - Pneumonitis caused by gold salt therapy: evidence for the role of cell-mediated immunity in its pathogenesis. *Am Rev Respir Dis*, 1980, 122, 145-152.
- Rees JH, Woodhead MA, Sheppard MN, du Bois RM. - Rheumatoid arthritis and cryptogenic organising pneumonitis. *Respir Med*, 1991, 85, 243-246.
- Yousem SA, Colby TV, Carrington CB. - Lung biopsy in rheumatoid arthritis. *Am Rev Respir Dis*, 1985, 131, 770-777.
- van Thiel, Robert J, van der Burg, Sicco, Groote, Alexander D, Nossent, George D, Willis, Stuart H. - Bronchiolitis obliterans organizing pneumonia and rheumatoid arthritis. *Eur Respir J*, 1991, 4, 905-911.