# BRONCHIOLITIS OBLITERANS*

## ROENTGENOLOGIC-PATHOLOGIC CORRELATION

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BRONCHIOLITIS obliterans is an end result of lower respiratory tract damage, in which bronchioles become obstructed by organizing exudate and polypoid masses of granulation tissue. Behind the obstructed bronchioles, fat-filled phagocytes may accumulate, forming an "obstructive," "golden," or "cholesterol" pneumonitis. In other cases, air-trapping predominates. Early roentgenographic recognition of this process may be invaluable to the patient, permitting diagnosis and treatment before irreversible changes develop.

The first reference to bronchiolitis obliterans was made by Reynaud in 1835.[26] It was not mentioned again in medical writings until 1901, when Lange[13] described 2 fatal cases of unknown origin. Since that time it has been described following toxic inhalations (war gas,[29] nitric, hydrochloric or sulfuric acid fumes,[3,14,18,22,24] talcum powder,[19] zinc stearate,[10] hot gases[23]), as a consequence of respiratory infections (including influenza,[30] measles,[5] whooping cough,[5] and adenovirus 21[4]) and also following inhalation of foreign bodies.[5] Microscopic descriptions of bronchiolitis obliterans have mentioned both the polypoid appearance of the organizing exudate[11,16,20] and also complete occlusion of the lumen with the final appearance of the bronchiole as a fibrous scar.[14,16,17,20] The surrounding parenchyma has sometimes been noted to be involved with an obstructive pneumonitis.[8] In other cases, surrounding zones of emphysematous alveoli have been described and attributed to bronchiolar obstruction with collateral ventilation.[6,25] These changes have been experimentally produced in dogs by exposure to chlorine,[29] phosgene,[29] and zinc stearate.[10] Intratracheal injection of nitric acid has produced the lesion in rabbits.[20] Some beneficial effect from steroids has been shown in animal experiments.[20] Improvement with steroid treatment in humans has been documented in silo-filler's disease.[14,21] Steroids have also been used in combination with other modes of treatment in patients recovering from bronchiolitis obliterans due to inhalation of hot gases[23] and also infectious disease.[9]

In the literature, many different roentgenographic appearances have been attributed to bronchiolitis obliterans. In the earliest reports, the pattern was usually described as miliary.[2,5,12] Cases secondary to known toxic inhalations generally showed a pattern suggesting pulmonary edema,[23,24] occasionally with zones of discrete nodularity. More recently, attention has been directed toward unilateral or bilateral hyperinflation, associated also with cylindrical or saccular bronchiectasis.[4,7] Cases with linear densities,[9] atelectasis,[9] granular and reticular infiltrates,[9] diffuse nodular patterns,[9] patchy bronchopneumonia[4] or lobar involvement[1] have been reported.

### MATERIAL

We reviewed all consultation cases filed under the diagnosis of bronchiolitis obliterans, bronchiolitis obliterans with interstitial pneumonia, chronic bronchiolitis, and cholesterol pneumonia. Of these, approximately 80 were selected as showing a major component of bronchiolitis obliterans on pathologic examination of surgical or

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Table I

SEX DISTRIBUTION

| Male | Female | Total |
|---|---|---|
| 34 (65%) | 18 (35%) | 52 |

AGE DISTRIBUTION

| | | |
|---|---|---|
| Less than 20 years | 7 | Range: 10 mo.–75 yr. |
| 20–39 | 5 | 80% of patients were |
| 40–59 | 26 | over 40 yr. |
| Over 60 years | 14 | |

autopsy material. We were able to obtain original roentgenograms or reproductions in 52 cases. These form the material for the clinical and roentgenologic analysis which follows. We are very much indebted to the physicians and radiologists who made roentgenograms and follow-up information available to us.

## CLINICAL FEATURES

Sixty-five per cent of the patients were males. The age distribution ranged from 10 months to 75 years, with 80 per cent (41) over 40 years of age (Table I). Onset was generally insidious, extending over a period of several weeks. The disease was treated empirically, on the average for an additional 2–3 months before biopsy and diagnosis. Only 1 patient was asymptomatic when the lesions were discovered roentgenologically. The most common clinical finding was cough, recorded in 39 out of 41 cases with adequate history. The next most common manifestation was dyspnea, which was specifically commented on in 36 out of 40 cases. Sputum production (25/32) and fever (22/35) were also frequent presenting signs. Rales were noted in 30 out of 36 cases with documented physical findings (Tables II and V). In 18 patients, the lesions of bronchiolitis obliterans appeared to be residual from an incompletely resolved pneumonia, but in 34 others, new or recurrent disease was indicated by clinical or roentgenologic findings. Surprisingly, only 11 patients had a history of chronic bronchitis or recurrent respiratory tract infection, including 3 asthmatics. Eight had histories of toxic inhalational exposure, including 3 cases of aspiration and 1 of acute exposure to nitric acid fumes (Table III). Ten patients had serious co-existing diseases, such as uremia, lymphoma or leukemia; or collagen diseases such as idiopathic thrombocytopenic purpura, rheumatoid arthritis or scleroderma (Table IV).

Table II

SYMPTOMS

| | Yes | No | Not Reported |
|---|---|---|---|
| Cough | 39 (95%) | 2 | 11 |
| Dyspnea | 36 (90%) | 4 | 12 |
| Sputum | 25 (78%) | 7 | 20 |
| Malaise | 18 (100%) | — | 34 |

Table III

PATHOGENESIS

| | |
|---|---|
| Post-pneumonic | 18 |
| Chronic pulmonary infection | 11 (3 with asthma) |
| Toxic inhalation | 8 (3 with aspiration) |
| Unknown etiology | 21 |
| Total | 58 (several patients with more than one known etiology) |

Laboratory findings were abnormal in many cases, but generally as nonspecific as the clinical findings. The white blood cell count was elevated above 10,000 per cu. mm. in 26 out of 41 cases. Bacterial or fungal culture of sputum was positive for respiratory pathogens in 14 out of 37 re-

Table IV

COEXISTING DISEASES

| | |
|---|---|
| Congestive heart failure | 2 |
| Lymphoma | 2 (1 with idiopathic thrombocytopenic purpura, 1 with diabetes) |
| Acute lymphocytic leukemia | 1 |
| Pulmonary alveolar proteinosis | 1 |
| Chronic glomerulonephritis (renal failure) | 1 |
| Scleroderma | 1 |
| Myasthenia gravis | 1 |
| Rheumatoid arthritis | 1 |

TABLE V

CLINICAL FINDINGS

| | Yes | No | Not Reported |
|---|---|---|---|
| Fever | 22 | 13 | 17 |
| Rales | 30 | 7 | 15 |
| White blood cells more than 10,000 mm.$^3$ | 26 | 15 | 11 |
| Positive sputum | 14 | 23 | 15 |

(6 *D. pneumoniae*, 2 *Candida*, 2 *Klebsiella*, 2 *Pseudomonas*, 1 *Staphylococcus*, 1 atypical AFB)

PULMONARY FUNCTION TESTS

| Restrictive | Obstructive | Normal | Not Reported |
|---|---|---|---|
| 9 | 7 | 6 | 29 |

ports. Eosinophilia (over 5 per cent) was noted in only 3 cases. Viral studies were rarely reported; none of these was positive. Pulmonary function data were available in 22 patients; a restrictive pattern was demonstrated in 9, and obstructive findings were noted in 7. Six patients had normal studies (Table v).

## ROENTGENOLOGIC FINDINGS

For purposes of classification, we have divided the roentgenologic findings into 3 main groups: *nodular densities* (18 cases); *alveolar opacities* (39 cases); and *hyperinflation* (2 cases). Several cases exhibited more than 1 of these patterns at different stages of the disease, and have been counted twice (Table VI).

TABLE VI

ROENTGENOLOGIC CLASSIFICATION

I. Nodular Densities (18 cases)
  a. Micronodular (less than 0.5 cm.) (5 cases)
  b. Discrete nodular (more than 0.5 cm.) (5 cases)
  c. Confluent nodular (6 cases)
  d. Lineonodular (5 cases)
II. Alveolar Opacities (39 cases)
  a. Bibasilar (10 cases)
    1. Diffuse (edema-like) (2 cases)
    2. Linear (atelectatic) (2 cases)
    3. Mixed (honeycomb) (6 cases)
  b. Other locations (29 cases)
    1. Lobar or segmental (20 cases)
    2. Diffuse (edema-like) (2 cases)
    3. Multiple irregular opacities (8 cases)
III. Hyperinflation (2 cases)

Lobar or Segmental Distribution (bibasilar excluded) (20 cases)

| | | | |
|---|---|---|---|
| Right upper lobe | 10 | Left upper lobe | 3 |
| Right middle lobe | 7 | Left lower lobe | 3 |
| Right lower lobe | 6 | | |

*Nodular densities* were subdivided into *micronodular* (distinct densities less than

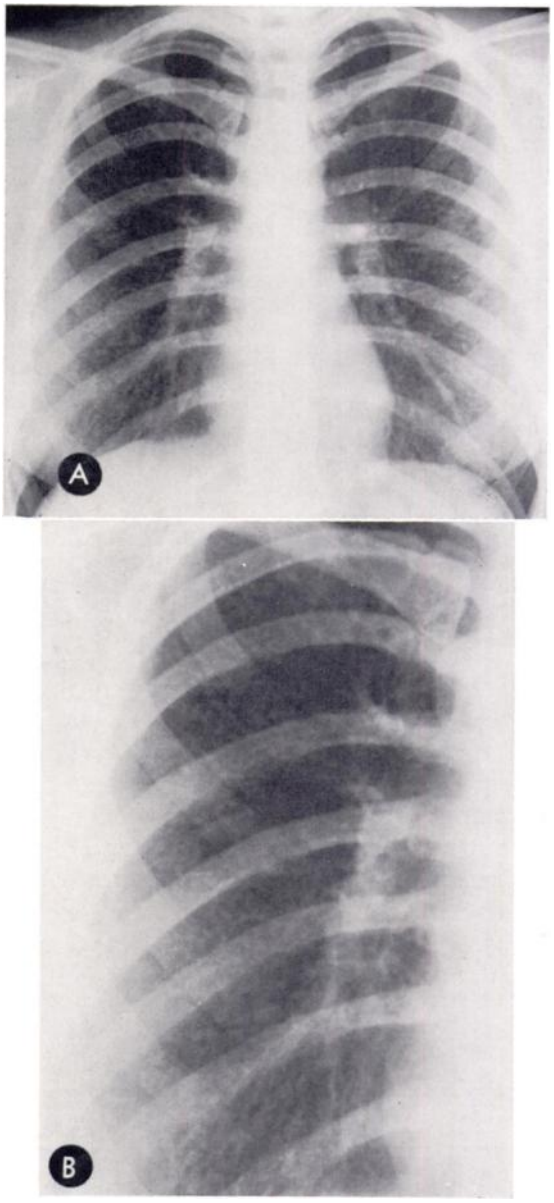


FIG. 1. (*A*) Posteroanterior (PA) roentgenogram of the chest. Micronodular pattern; 18 year old female. Dyspnea for 1 month. (*B*) Detail, same patient.

0.5 cm. in diameter [5 cases]) (Fig. 1, *A* and *B*); *discrete nodular* (distinct densities greater than 0.5 cm. in diameter [5 cases]) (Fig. 2); *confluent nodular* (consolidations with a nodular pattern visible in less involved peripheral regions [6 cases]) (Fig. 3, *A* and *B*); and *lineonodular* (fine linear or reticular markings in addition to micronodular densities [5 cases]) (Fig. 4).

The *alveolar opacities* included varying degrees of atelectasis or consolidation, both subsegmental and lobar, sometimes with patchy involvement of both lungs. Of these, 10 cases had predominantly *bibasilar* involvement: *diffuse* (2 cases) (Fig. 5), *linear* (2 cases) (Fig. 6), or *mixed* forms, including reticular or honeycomb patterns, (6 cases) (Fig. 7). The remaining 29 cases included a preponderance of *segmental* or *lobar* consolidation and atelectasis (20 cases) (Fig. 8). The distribution, not counting the bilateral basilar group, included 10 cases with *right* upper lobe involvement, 7 with *right* middle lobe and 6 with *right* lower lobe findings, but only 3 with *left* upper lobe and 3 others with *left* lower lobe disease. Ten other cases of alveolar opacity were divided into: 2 with diffuse alveolar opacification like central pulmonary edema (Fig. 9); and 8 with multiple irregular opacities (Fig. 10, *A* and *B*). These included a mixture of shadows which individually varied from irregular nodules to segmental consolidation; some were unchanged on serial roentgenograms, while in other cases the irregular densities disappeared and re-appeared in different places (Fig. 10, *A* and *B*; and 18, *A–C*).

Hyperinflation was noted in 2 children (Fig. 11, *A* and *B*), in 1 of whom it later disappeared; the hyperinflation of preexisting emphysema was excluded from

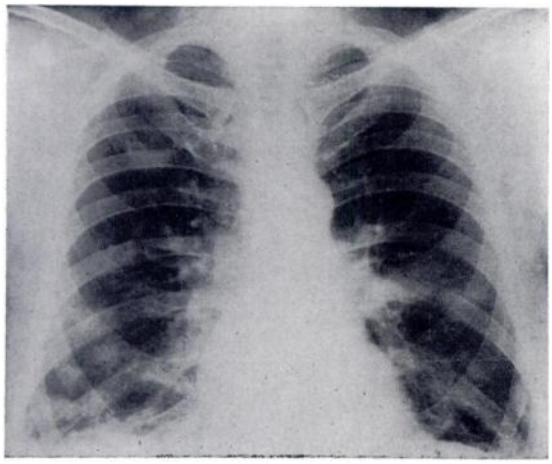

Fig. 2. PA chest. Discrete nodular pattern; 45 year old male. Cough and sputum for 4 months.

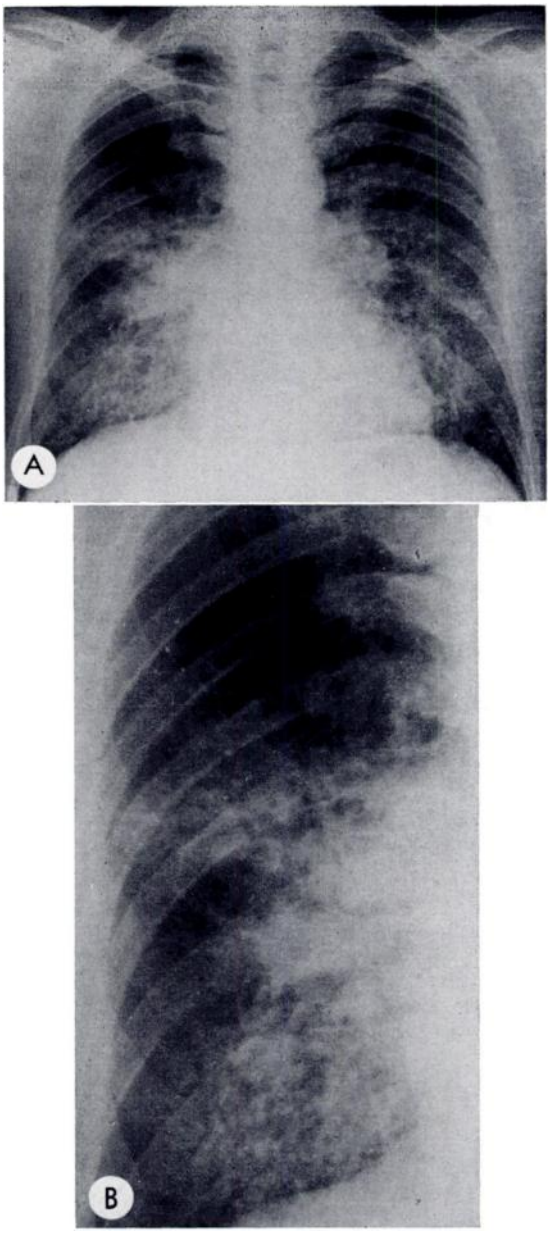


Fig. 3. (*A*) PA chest. Confluent nodular pattern; 49 year old male. Cough, fever, sputum for 2 months. (*B*) Detail, same patient.

Hyperinflation was noted in 2 children (Fig. 11, *A* and *B*), in 1 of whom it later disappeared; the hyperinflation of pre-

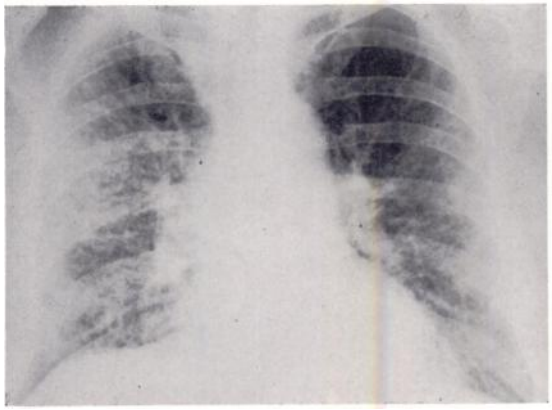

Fig. 4. PA chest. Lineonodular pattern; 65 year old male. Fever for "several weeks."

this category. In only 1 case was hilar lymphadenopathy identified: a child with chronic pulmonary infection.

Additional diagnostic roentgenographic procedures, such as tomography, bronchography, arteriography, or lung scanning were rarely employed in our series of patients. Useful additional information was not provided by these studies, when they were available.

Bronchiectasis was not a prominent feature in those cases in which it was sought bronchographically; there was cylindrical bronchial dilatation demonstrated in 1 case of segmental disease; in addition, several cases showed bronchiolectasis pathologically.

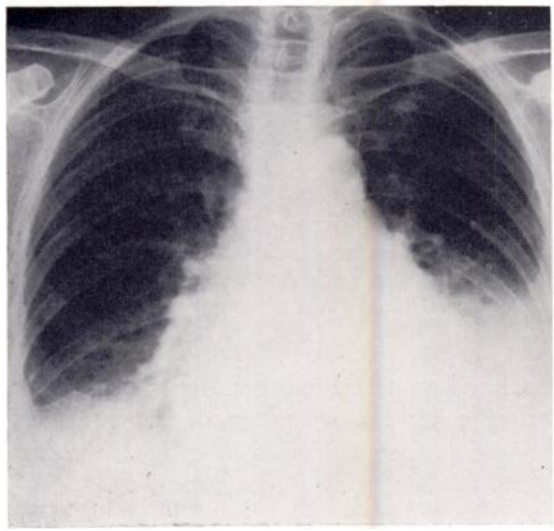

Fig. 5. PA chest. Diffuse bibasilar pattern; 71 year old female. Dyspnea for several months.

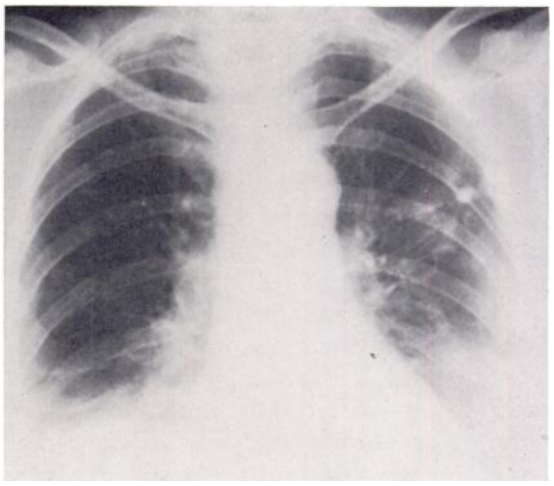

Fig. 6. PA chest. Linear bibasilar pattern; 50 year old female. Fever, cough and malaise for 4 months.

### Roentgenologic Differential Diagnosis

Some of the patterns were clearly more distinctive than others. The *micronodular* and *lineonodular* patterns were similar to those in diffuse infectious granulomatous disease or occupational lung disease, or possibly pulmonary sarcoidosis. In bronchiolitis obliterans the nodules were less distinct than in most cases of these dis-

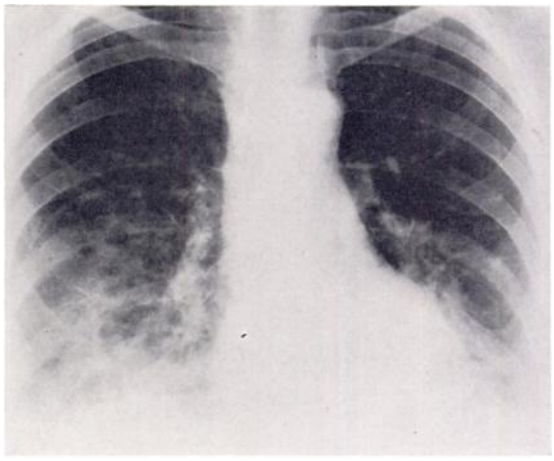

Fig. 7. PA chest. Mixed bibasilar pattern; 53 year old female. Cough, dyspnea and malaise for 4 months.

eases. The *discrete* and *confluent nodular* densities suggested other less common diseases, such as diffuse or localized vasculitis, multiple abscesses due to necrotizing pneumonia or sepsis, or carcinomatosis, either disseminated bronchiolo-alveolar cell carcinoma or metastatic. The *basilar opacities* were suggestive of chronic interstitial pneumonia, and this indeed may have coexisted in some cases. The roentgenologic findings in most cases, however, suggested only chronic or recurrent pneumonia and atelectasis, with aspiration an important possibility. These were manifest as *segmental* or *lobar* consolidation or atelectasis. Unilateral hyperinflation or "unilateral hyperlucent lung" (Swyer-James[28] or MacLeod's[15] syndrome) is usually diagnosed without difficulty by both radiologist and clinician, so that such patients rarely come to biopsy. This may account for the small number of cases with hyperinflation in our series.

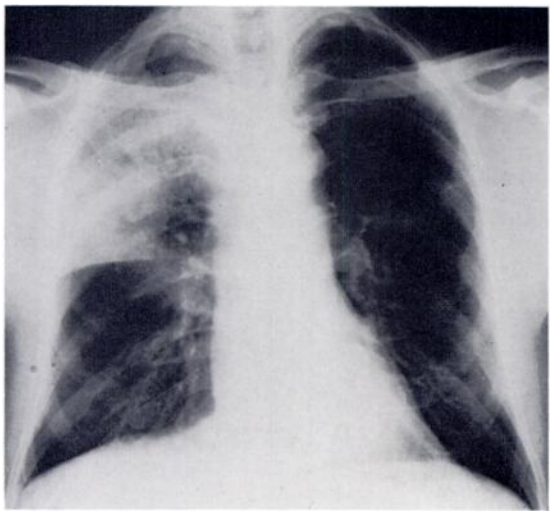

Fig. 8. PA chest. Lobar consolidation pattern; 64 year old male. Proven hiatal hernia with aspiration. (See also Fig. 20.)

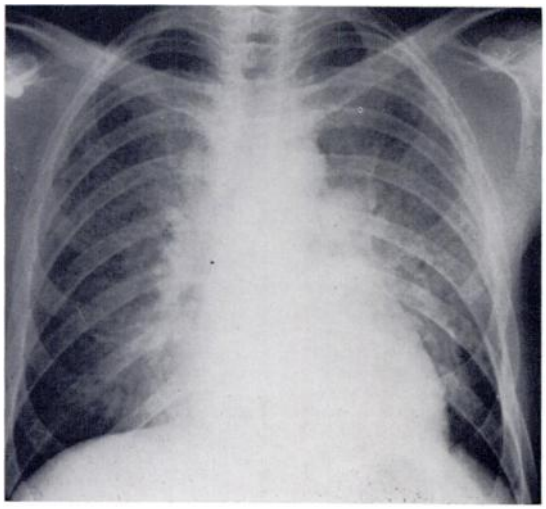

Fig. 9. PA chest. Diffuse alveolar opacity pattern; 26 year old male. Uremia with 2 week history of fever, cough, dyspnea, malaise. (See also Fig. 19.)

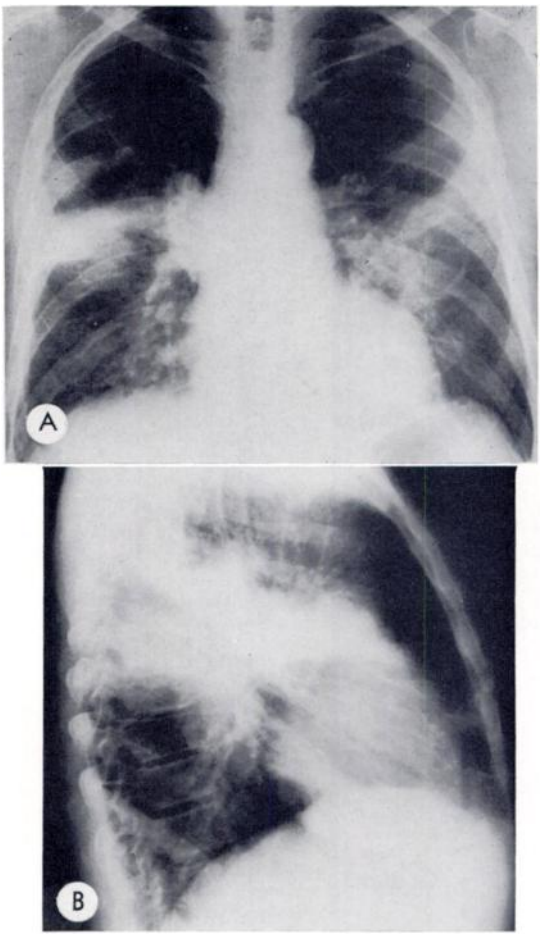


Fig. 10. (*A*) PA chest. Multiple irregular opacity pattern; 68 year old male. Recent onset of cough, sputum, dyspnea, malaise. (*B*) Lateral, same patient. (See also Fig. 18.)

### PATHOLOGIC FINDINGS

The diagnosis was established as a result of surgical biopsy in 49 cases, with complete

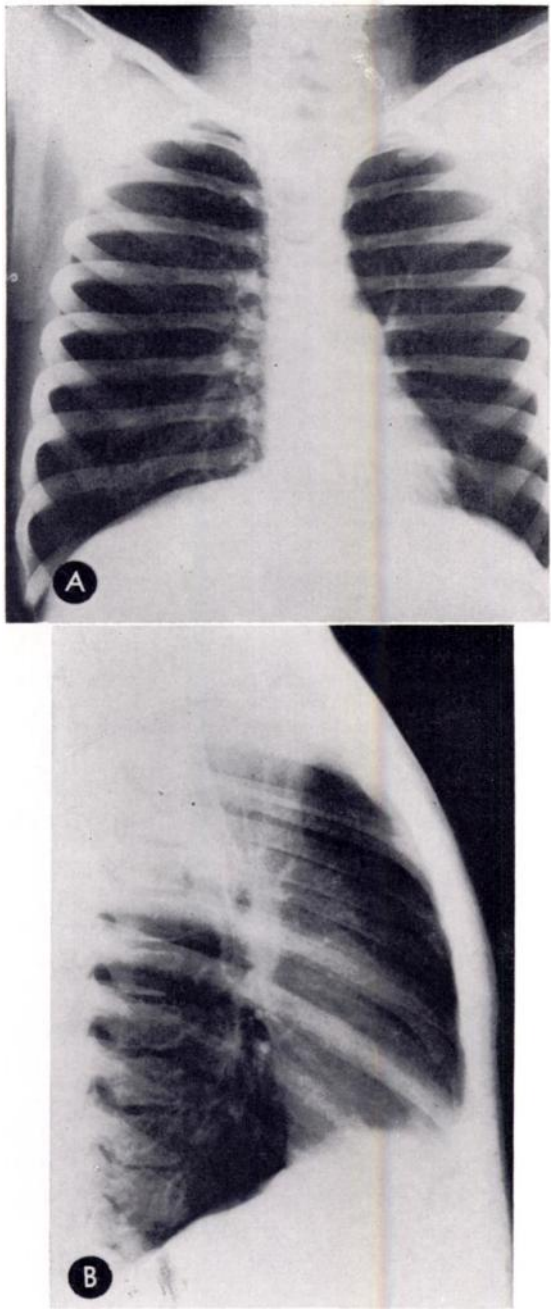


FIG. 11. (*A*) PA chest. Hyperinflation pattern; 10 year old male. Four month history of fever and cough. (*B*) Lateral, same patient.

excision of the roentgenographically abnormal region in 7 cases. (Two of these later developed disease involving other lobes.) In 3, the diagnosis was first made at autopsy; 7 other patients from this series came to autopsy for various reasons.

Bronchiolitis obliterans was manifest in several principal ways. Most commonly the respiratory bronchioles were filled with characteristic masses of organized exudate, histologically resembling nasal polyps (Fig. 12, *A* and *B*). Less frequently, peribronchial and mural infiltration by mononuclear cells and granulation tissue resulted in a constrictive bronchiolitis (Fig. 13). Least common in this series, and most difficult to detect on casual histologic examination, was total or subtotal obliteration of the bronchioles by scar (Fig. 14).

Other features varied according to the chronicity of the process, and whether it was diffuse or focal. The intrabronchiolar polyps were initially cellular, with lymphocytes and mononuclear cells predominating in a matrix of proteinaceous exudate rich in fibrin. Some also contained polymorphonuclear leukocytes. More "mature" polyps consisted of somewhat myxoid connective tissue containing fibroblasts. In some cases, central nests of plasma cells, lymphocytes and large mononuclear cells often replete with residual bodies were seen in many of the polyps. Many polyps were covered with respiratory epithelium, and some were converted into mounds of granulation tissue with a broad mural attachment encroaching on the small bronchioles (Fig. 15). In other regions the original lumen was converted into several channels, each lined by epithelium or obliterated completely by fusion of the polyp with the walls of the airway. The polypoid masses extended into alveolar ducts and alveoli to a variable extent, but were quite rare in small bronchi. Polypoid connective tissue proliferation was uncommon in cases with infiltrative or constrictive bronchiolitis.

The condition of the nearby airways varied from clear and overdistended (Fig. 14) to partly consolidated with severe interstitial thickening. The alveoli were filled with a variety of cellular constituents, but most notably with fat-filled phagocytes (Fig. 16). These foamy cells could be found in small numbers even in alveoli with relatively normal septa as well as in those alveoli with interstitial fibrosis and mono-

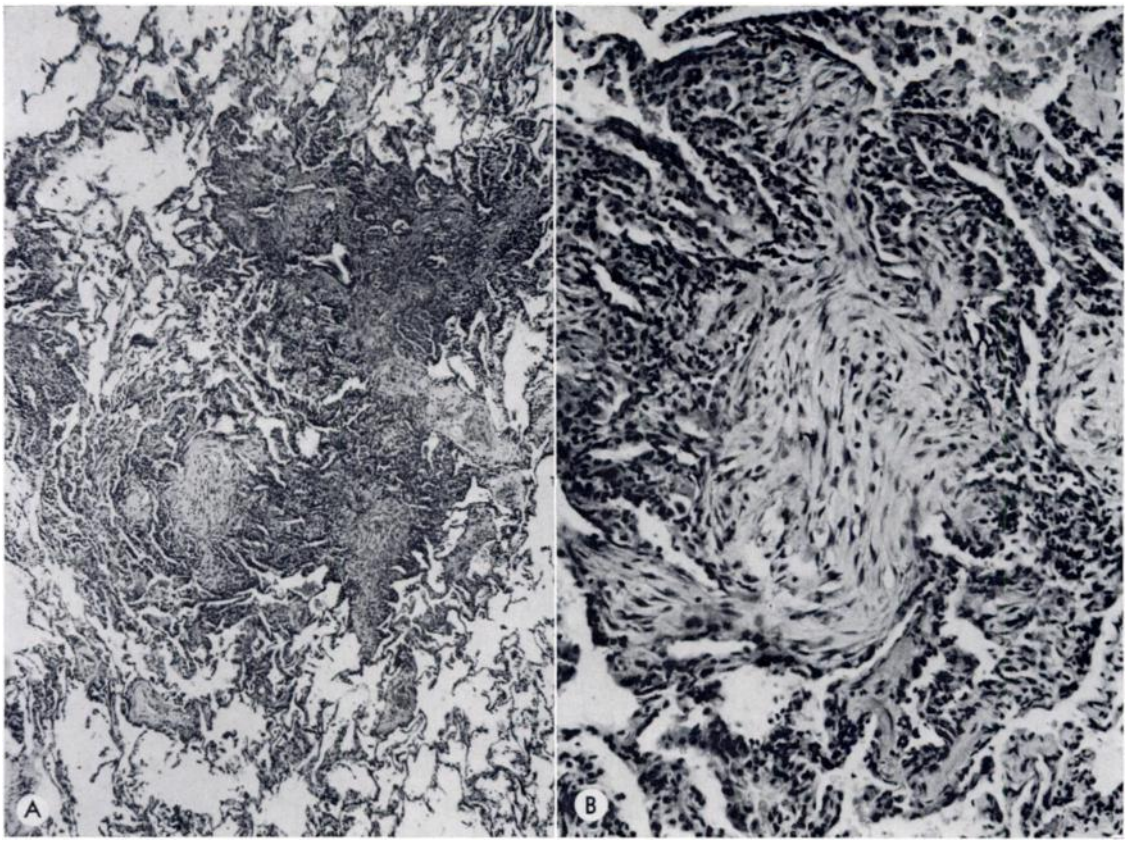


Fig. 12. (*A*) Low power photomicrograph. Intrabronchial and adjacent interstitial organization. Note normal alveoli in periphery of acinus (50×). (*B*) Detail, same field. Polypoid mass of organizing exudate filling bronchiole, the typical lesion (200×).

nuclear infiltration where they were more numerous, often aggregated into masses. In some foci the fat-filled mononuclear cells were found in large accumulations within the thickened walls of distal air spaces and occasionally within the intrabronchiolar polyps. In several cases large mononuclear cells released enough cholesterol for the characteristic acicular crystals to appear; in at least 1 case there was a marked giant cell reaction to the endogenous cholesterol. "Cholesterol" or "obstructive" or "endogenous lipid" pneumonia is often an important feature of bronchiolitis obliterans, sometimes so marked as to be confused with pneumonia due to exogenous lipid.

Interstitial infiltration with lymphocytes, plasma cells, and occasionally eosinophils was usually localized in the vicinity of the involved bronchioles (Fig. 12, *A* and *B*). In some cases interstitial infiltration appeared to be the predominant lesion, much more widely distributed than the bronchiolitis obliterans, suggesting that the latter was a complication of a diffuse interstitial pneumonia. Honeycombing, or end-stage scarring of the lung, was seen in 4 cases, although it was early and focal in 2. In many cases of severe interstitial pneumonitis of the usual type there is some bronchiolitis obliterans present, but these cases are not considered here. One case with interstitial pneumonia had many small granulomas, typical of hypersensitivity, in this case attributable to exposure to pigeons. Several other cases had occasional small granulomas; 1 had numerous sarcoid lesions causing bronchiolar obstruction.

One case in a child with focal total obliteration of bronchioles had diffuse pul-

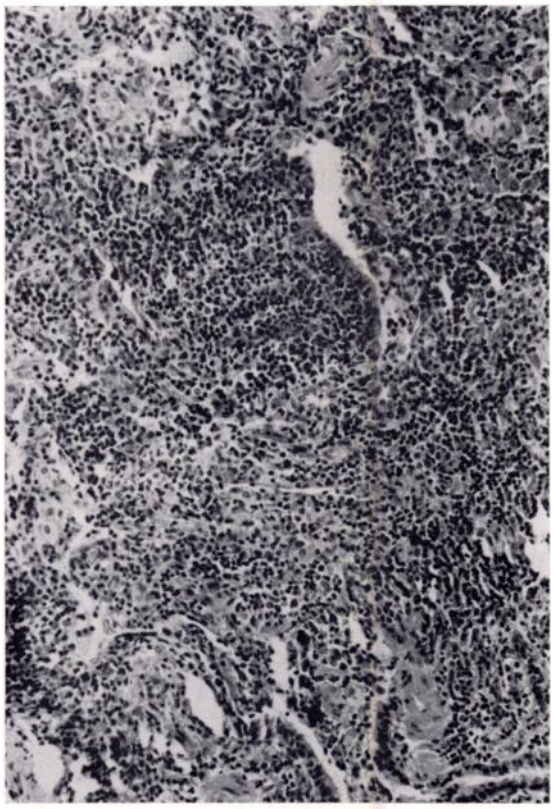

Fig. 13. Constrictive bronchiolitis. Note extensive peribronchial and mural infiltration by mononuclear cells and lymphocytes (200×).

monary hyperinflation and an "emphysematous" appearance. This may be considered bilateral "radiolucent lung" syndrome[15,28] in a child (Fig. 14). These findings were consistent with the bronchiolar obstruction described in several cases studied pathologically.[25] Another case with similar histologic findings did not show overinflation of the lungs, but the roentgenograms also under-represented the severity of parenchymal damage as suggested by severe functional impairment. Some small airways could be detected only as scars adjacent to small pulmonary arteries (Fig. 14); in others there was "recanalization" (Fig. 17) with one or more epithelial-lined channels, such as with organization in arterial thrombosis. Another case with such obliterative changes had an infiltrative bronchiolitis, but typical polyps and some evidence of bronchiolectasis in various regions.

## Roentgenologic-Pathologic Correlation

There is no direct correspondence between roentgenographic patterns and histologic findings to be found in this material. The advantage of surgical biopsy material for these studies, in being free of the usual terminal or aspiration pneumonia and the damage from respirator treatment with oxygen, is balanced by the disadvantage of restricted sampling of the lung. While a small biopsy may reveal the pathogenesis of the pulmonary disease, it often does not explain the distribution of findings seen roentgenologically. A further sampling problem is the absence of small and large bronchi in most biopsies. Although the discussion here centers on bronchiolitis obliterans, the extent of disease further

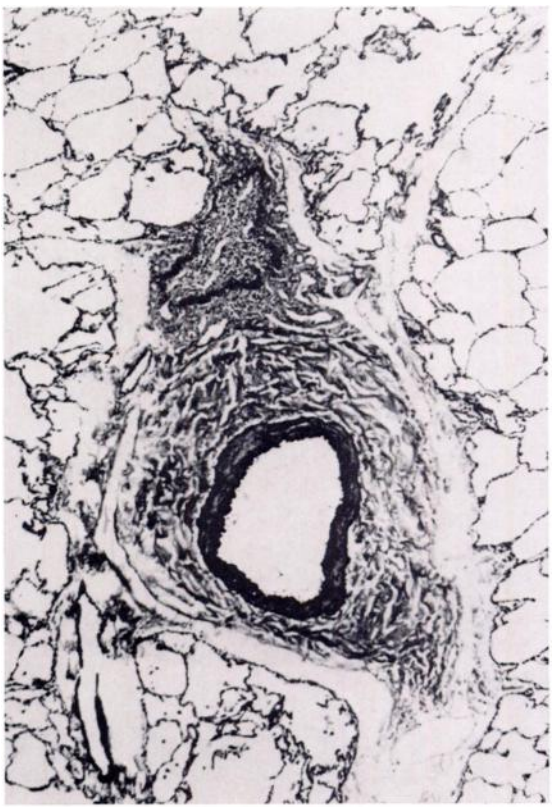

Fig. 14. Total focal bronchiolar obliteration (elastic tissue stain). The shrunken bronchiole, adjacent to a patent pulmonary arteriole with adventitial fibrosis, is outlined by its elastica. Note surrounding hyperinflated parenchyma, evidence of collateral ventilation (80×).

proximal would clearly affect the roentgenologic distribution of findings. Nodules demonstrable roentgenologically in this disease were usually 2–3 mm. in size (micronodular or lineonodular) or just under 1 cm. in size (discrete nodular). Nodules of appropriate size were not always demonstrated in the histologic material from these cases, although round infiltrates were seen on many slides from the entire series. It must be conjectured that micronodular shadows represent the focal interstitial infiltration and intra-alveolar accumulation of exudate including the fat-filled phagocytes around an obstructed respiratory bronchiole, but not the entire acinus represented by the discrete nodular shadow. The lineonodular patterns were almost all associated with considerable interstitial pneumonia or fibrosis, although half the micronodular cases were as well.

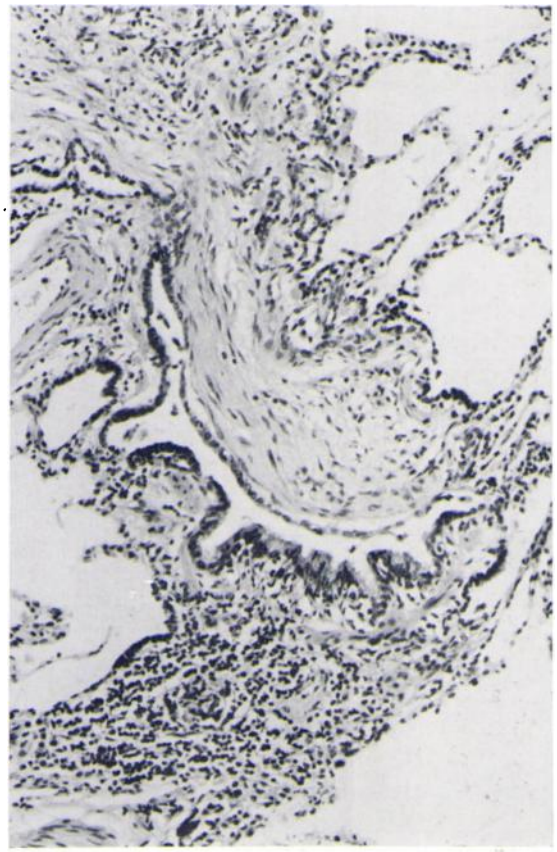

FIG. 15. Organized polypoid mass covered by respiratory epithelium encroaching on the lumen of a bronchiole. Healing stage, although lymphocytic infiltrate persists (200×).

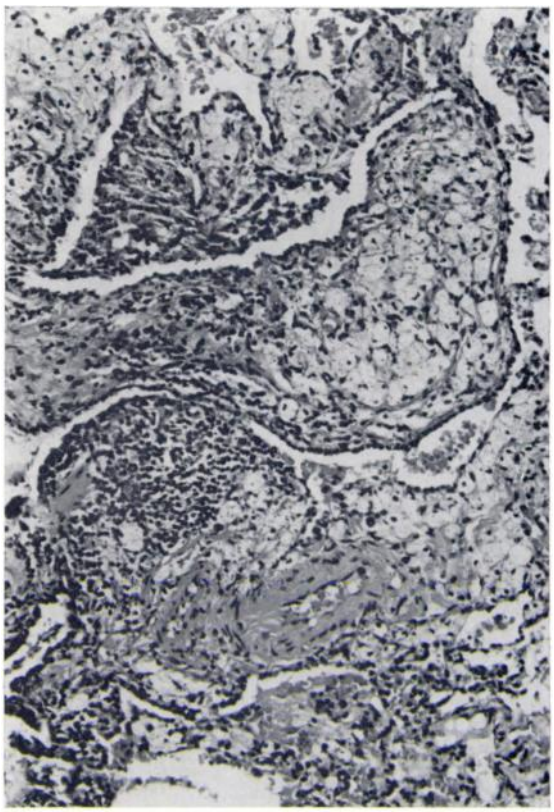

FIG. 16. Abundant fat-filled phagocytes, many incorporated into interstitium by overgrowth of epithelium (200×).

The large number of cases with atelectasis or segmental and lobar opacification suggests that many small and subsegmental bronchi were also filled with organized exudate, although this could not be documented in this material. Few of these cases had significant interstitial fibrosis aside from focal changes around obstructed bronchioles. In a search for means of identifying cases with a hypersensitivity component, histologic findings of abundant plasma cells or acid mucopolysaccharides were compared with the roentgenologic pattern or clinical syndrome. There was no correlation between these findings and either the roentgenographic pattern or over-all course. The finding of small granulomas, sarcoid-like, also failed to pinpoint any particular syndrome or roentgenologic pattern in the majority of the 8 cases. Finally, the focal scarring of airways with

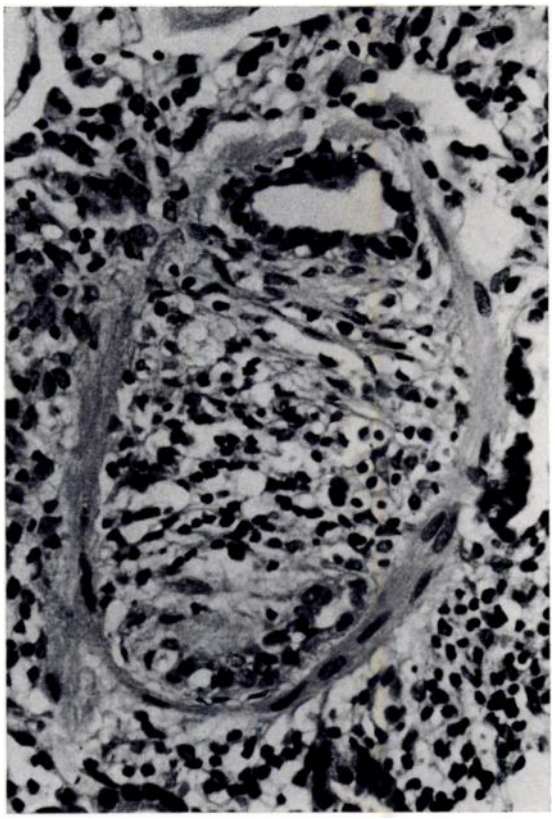

FIG. 17. Partial recanalization of occluded bronchiole. Note original size indicated by persistent smooth muscle outline (500×).

adjacent alveolar overexpansion matched the roentgenographic appearance of pulmonary hyperinflation in 1 case, but correlated poorly in the other case of roentgenographic hyperinflation, or the other cases with histologic evidence of focal air-trapping.

### CLINICAL COURSE AND THERAPY

In patients who developed bronchiolitis obliterans, the etiology could be classified into one of 4 major categories: (1) post-pneumonic; (2) chronic or recurrent respiratory disease; (3) toxic inhalation (including aspiration); and (4) unknown etiology.

In our series, there were 18 patients in the post-pneumonic group. These individuals were generally in good health until sudden onset of a lobar or subsegmental pneumonia. When the pneumonia failed to clear adequately with treatment, lung biopsy was obtained and bronchiolitis obliterans was recognized as a component of the disease. In these cases, bronchiolitis obliterans was obviously secondary to bacterial or viral infection. There was some overlap with the chronic respiratory disease category.

The second group included 11 patients with lifelong histories of chronic bronchitis, asthma, or recurrent respiratory tract infections. As previously noted, 3 of these patients were also classified in the post-pneumonic group.

In the third group there were 8 cases of toxic inhalation, only 1 being acute. This patient, exposed to nitric oxide fumes, had the typical biphasic course consisting of rapid onset of pulmonary edema clearing spontaneously, followed by a lag period of 1–2 weeks and succeeded by an even more intense and longer-lasting episode of diffuse alveolar opacities and respiratory distress. This pattern has been fully described elsewhere.[18,27] Four of these patients had co-existent major disease.

The fourth group included many patients, who could not be classified in any definite category; the nature and etiology of the disease were unclear from the start. Clinical and laboratory observation were of little help in elucidating the cause of the patients' symptoms. These patients were treated largely on an empirical basis.

Eleven deaths occurred among the 52 patients, 7 in individuals with no known etiology for their disease. Five of these patients showed nodular densities on their roentgenograms, and 3 demonstrated a segmental or lobar pattern.

In addition to symptomatic treatment and respiratory support, where necessary, many patients were treated with a variety of antibiotics, steroids or combinations of the 2. We have specific information relating to such treatment in 40 patients (Table VII). Of 17 patients treated with steroids alone, 15 showed partial or complete (6) improvement. Of 5 treated with antibiotics alone, 3 showed improvement (1 complete). Of 18 patients treated with a combination

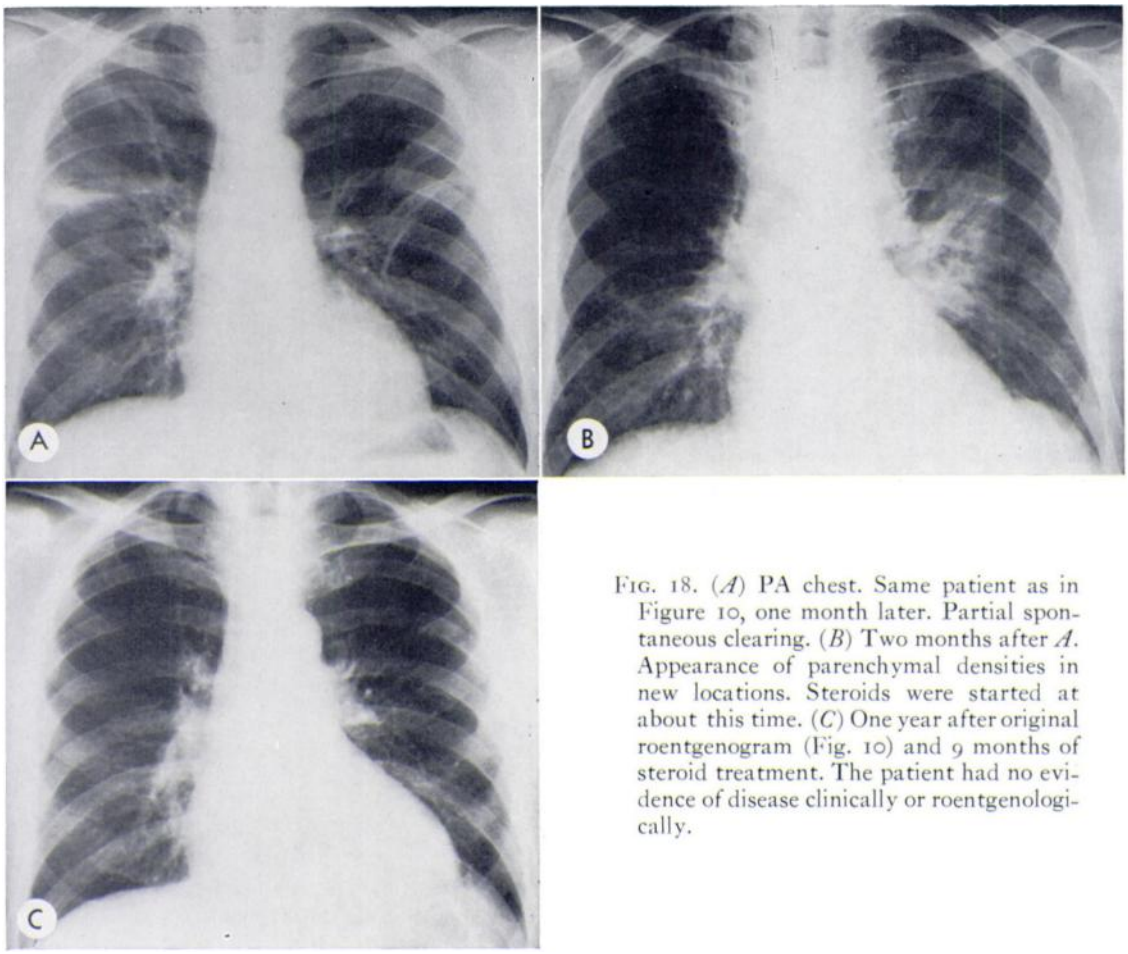


Fig. 18. (*A*) PA chest. Same patient as in Figure 10, one month later. Partial spontaneous clearing. (*B*) Two months after *A*. Appearance of parenchymal densities in new locations. Steroids were started at about this time. (*C*) One year after original roentgenogram (Fig. 10) and 9 months of steroid treatment. The patient had no evidence of disease clinically or roentgenologically.

of antibiotics and steroids, 10 improved (5 complete).

Of 11 patients with post-pneumonic disease, 3 showed improvement with steroids alone, and 1 improved with antibiotics alone. When combination therapy was employed, 3 patients improved, 4 demonstrated no change. Seven underwent complete excision of the affected area (5 with no other treatment), but of these only 1 recovered completely. Two of these patients died shortly afterwards, 2 showed continuing disease in other sites. In 2 more, there was no follow-up.

Of the 11 chronic pulmonary disease patients, 3 improved with steroids alone and 1 with antibiotics alone. Of 6 patients treated with the combination, 5 improved. In another patient the lesion was resected with disease developing later in another lobe.

In the toxic inhalation category no patients were treated with antibiotics alone. Of the total of 8 patients, 2 were given steroids alone (1 improved) and 5 were given the combination of medications (3 improved). One patient had resection of his lesion; however, he died shortly afterwards.

Of 21 patients with bronchiolitis obliterans of unknown etiology, 3 patients were given combination treatment 1 improved and 2 died. Four patients were given antibiotics alone and 1 showed complete improvement. Two died, 1 after temporary improvement. Nine patients were given steroids alone and 7 showed lasting improvement (Fig. 18, *A C*). One showed

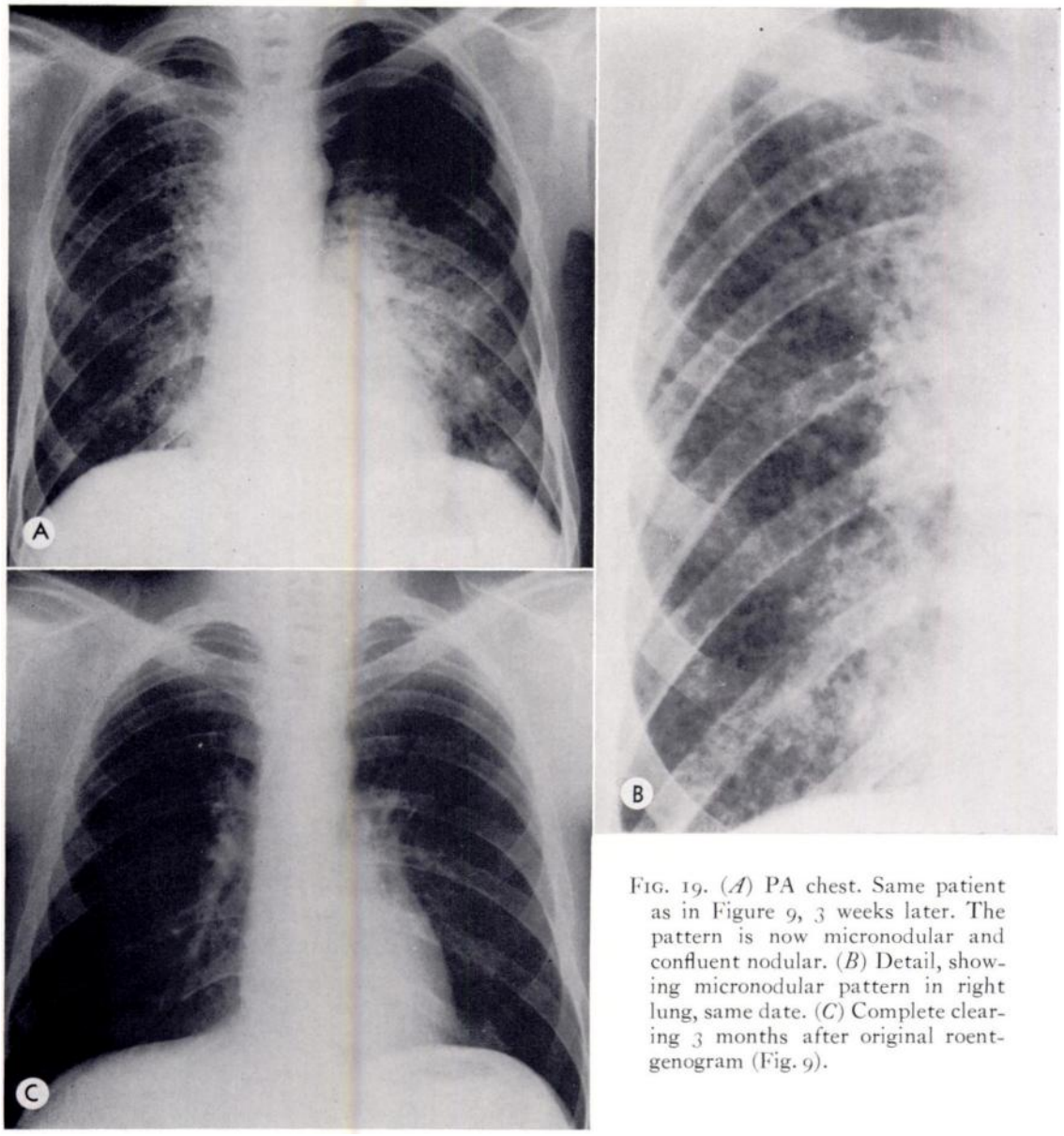


Fig. 19. (*A*) PA chest. Same patient as in Figure 9, 3 weeks later. The pattern is now micronodular and confluent nodular. (*B*) Detail, showing micronodular pattern in right lung, same date. (*C*) Complete clearing 3 months after original roentgenogram (Fig. 9).

temporary improvement, but later died. Of 4 patients receiving no specific treatment, 2 improved.

Thus it is clear that steroids may be of considerable benefit, even in the absence of a significant component of proven hypersensitivity.

### Correlations between roentgenographic patterns and clinical course

Some interesting relationships were noted between the roentgenographic pattern and the clinical course (Table VIII). Cases with a *micronodular* roentgenographic pattern fell into 2 classes clinically. Three of the 5 patients had symptoms and roentgenologic findings which cleared readily on steroids or antibiotics, without evidence of residual disease. Two patients appeared much more severely affected, and also had more prominent pulmonary infiltration roentgenologically. One of these died, and had evidence of *Klebsiella* infection at postmortem ex-

TABLE VII

RESPONSE TO THERAPY

| Pathogenesis | Steroids | Antibiotics | Combination | Surgery | No Specific Treatment |
|---|---|---|---|---|---|
| Post-pneumonic (18 patients) | PI (2) (1 with later resection)<br>CI (1) | PI (1) (also in chronic infection category) | PI (1)<br>CI (2) (1 complete hiatal hernia repair*)<br>NC (4) (1 with later resection and death) | Resected: 5 (1 death, 1 CI, 2 CD, 1 no FU) | 1 CD, 1 no FU |
| Chronic pulmonary infection (11 patients) | PI (2)<br>CI (1) | PI (1) (also in post-pneumonic category) | PI (3)<br>CI (2) (1 complete hiatal hernia repair*)<br>NC (1) (also in post-pneumonic category) | Resected: 1 CD (also in post-pneumonic category) | |
| Toxic inhalation (including aspiration; 8 patients) | PI (1)<br>NC (1) | | PI (1)<br>CI (2) (1 complete hiatal hernia repair*)<br>Death (2) | Resected: 1 (death) (also in post-pneumonic category) | |
| Unknown etiology (21 patients) | PI (4) (1 improved temporarily, death later)<br>CI (4) (1 later unrelated death)<br>NC (1) | PI (1) (improved temporarily, death later)<br>CI (1)<br>NC (1)<br>Death (1) | CI (1)<br>Death (2) | | 4 (2 CI, 1 death, 1 no FU) |

PI = partial or temporary improvement; CI = complete improvement; CD = continuing disease; FU = follow-up; NC = no change; * = same patient.

amination; the other had pre-existing uremia, but nevertheless recovered after a stormy course (Fig. 19, *A–C*).

The 5 patients with *lineonodular* opacities were consistent in having a longer history of active disease. Improvement was obtained by treatment with steroids and antibiotics together in most cases, but in 4 with follow-up there was residual clinical or roentgenologic abnormality.

The effects of disease were more severe in patients with *discrete nodular* or *confluent nodular* densities on chest roentgenograms. Only 2 of the 9 patients (2 fell into both categories) in these categories recovered completely; 5 died, and 1 is chronically ill at this time. One patient had no follow-up reported.

In the groups with *basilar opacities* and *multiple irregular* or *diffuse alveolar opacities*, there were few cases of complete recovery among those with adequate follow-up (6/15). Nearly all those with substantial improvement had been treated with steroids (4/6). In the group with *lobar* or *segmental* disease, 7 had removal of diseased lung by surgery with 2 postoperative deaths and 2 others with continuing or recurrent lung involvement (Fig. 20). One showed complete improvement. About half of those treated primarily by medical means either died or had residual lung disease; only 1 patient had apparently com-

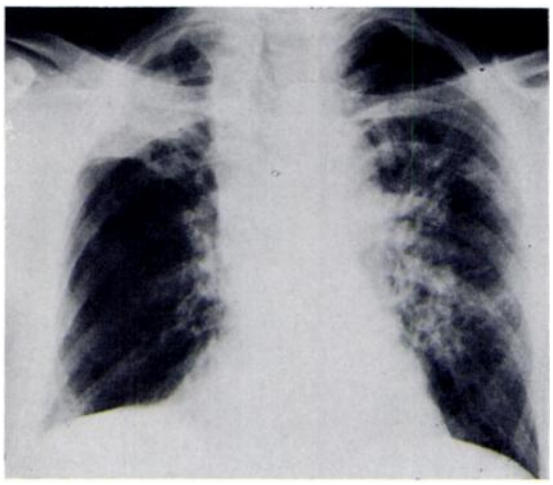

FIG. 20. PA chest. Same patient as in Figure 8, 5 months later. Involvement of additional parts of the lungs in patient with recurrent aspiration. The chest roentgenogram cleared completely on a combination of antibiotics and steroids, following a hiatal hernia repair.

TABLE VIII

RELATIONSHIP BETWEEN ROENTGENOGRAPHIC PATTERN AND CLINICAL COURSE

| | Complete Improvement | Continuing Disease and/or Residua | Death | No Follow-up |
|---|---|---|---|---|
| Micronodular | 4 (1 overlap with diffuse opacities) | 0 | 1 (1 overlap with confluent nodular) | 0 |
| Discrete nodular | 0 | 1 (1 overlap with lobar) | 3 (2 overlap with confluent nodular) | 1 (overlap with basilar opacities) |
| Confluent nodular | 2 | 0 | 4 (2 overlap with discrete nodular; 1 overlap with micronodular) | 0 |
| Lineonodular | 0 | 4 (1 overlap with multiple opacities; 1 overlap with lobar) | 0 | 1 |
| Bibasilar | 3 | 4 | 1 | 2 (1 overlap with discrete nodular; 1 overlap with lobar) |
| Lobar or segmental | 2 (1 overlap with multiple opacities) | 9 (1 overlap with discrete nodular; 1 overlap with hyperinflation; 1 overlap with lineonodular) | 3 | 6 (1 overlap with bibasilar opacities) |
| Diffuse (edema-like) | 1 (overlap with micronodular) | 0 | 1 | 0 |
| Multiple opacities | 2 (1 overlap with lobar) | 2 (1 overlap with lineonodular) | 1 | 3 |
| Hyperinflation | 0 | 2 (1 overlap with lobar) | 0 | 0 |
| Total | 12 (2 overlap) | 18 (4 overlap) | 11 (3 overlap) | 11 (2 overlap) |

plete recovery, without lung resection, and this was after hiatal hernia repair in addition to medical treatment. Follow-up was insufficient in 6 others. These figures suggest that even apparently localized disease was not readily treated with success, and that a significant number of patients develop new manifestations of pulmonary disease eventually (Fig. 10, *A* and *B*; and 18, *A–C*).

Attempts to correlate the roentgenographic patterns with the pathologic findings failed to yield significant results. This may be because the lung specimens represented many different stages of organization, as well as somewhat varied manifestations of bronchiolar obstruction, and only few showed obviously irreversible bronchial scarring or parenchymal honeycombing. It was also difficult to tell if a lung biopsy was representative of the predominant pattern of lung involvement. Since etiology was obscure in the great majority of cases, there was no convenient bridge between pathologic and clinical manifestations or roentgenographic findings.

## SUMMARY

Bronchiolitis obliterans is a pathologically defined syndrome of bronchiolar ob-

struction by organizing exudate, often associated with cholesterol and interstitial pneumonia.

Among 52 cases with roentgenograms available for review, few were associated with specific etiologic factors. Several patients had co-existent systemic disease.

Although occasionally a localized process amenable to surgery, bronchiolitis obliterans was usually diffuse, causing pulmonary insufficiency and death in some, but resolving in others.

Administration of steroids was usually associated with clinical improvement.

Roentgenologic patterns included: nodular densities (micronodular, discrete, confluent and lineonodular); alveolar opacities (diffuse, multiple irregular or bibasilar); and hyperinflation.

Early recognition of this syndrome may permit treatment before irreversible changes develop.

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