MULTIPLE BRONCHOSTENOSES DUE TO SARCOIDOSIS

REPORT OF TWO CASES

BY

MICHAEL HONEY, M.B., M.R.C.P.

University College Hospital, London;
Formerly Medical Registrar, Brompton Hospital

AND

EWART JEPSON, M.B., M.R.C.P.

Medical Registrar, Westminster Hospital;
Formerly House-Physician, Brompton Hospital

We have recently seen two patients with multiple bronchial stenoses. Bronchoscopic biopsy revealed non-caseating epithelioid follicles, the tuberculin test was negative, and tubercle bacilli were absent from the sputum. We present the case report of these two patients with our reasons for believing them to be suffering from sarcoidosis, discuss the symptoms which led to their investigation, and briefly review previous reports of bronchial sarcoidosis.

Intrathoracic sarcoidosis usually affects the pulmonary parenchyma, where lesions occur mainly in the region of small lymphatics in the peribronchial, perivascular, and subpleural areas (Longcope and Freiman, 1952), and the hilar and paratracheal lymph nodes. In the literature there are few references to bronchial lesions in sarcoidosis. The bronchi may be involved in one of three ways. Firstly, enlarged hilar nodes may compress major bronchi, with resulting atelectasis of lobe or segment (Snapper and Pompen, 1938; Turiaf and Brun, 1955) or bronchiectasis (Cowdell, 1954); this is unusual, and there are no reports of hilar nodes ulcerating through the bronchial wall, as occurs in primary tuberculosis. Secondly, the fibrotic process in the later stages of the disease may constrict bronchi, and fibrosis in the region of the hilum may lead to progressive distortion and narrowing of the major bronchi: a case in which this occurred is described by Longcope and Freiman (1952), who, in their review of 160 cases of sarcoidosis, state that this is not infrequent. Thirdly, sarcoid lesions may occur in the bronchial wall; we have discovered 13 such cases in the literature, characterized by the presence of mucosal abnormalities, bronchial stenoses, or both, and the finding of sarcoid follicles on histological examination of biopsy or necropsy specimens. We believe that the two cases reported here fall into this group.

Case 1

A brewery engineer aged 36 first attended Brompton Hospital in October, 1950. His illness began in July, 1948, with a febrile episode, when a chest radiograph showed an opacity in the anterior segment of the right upper lobe. This opacity cleared in 10 weeks and his symptoms subsided. In 1949 he developed increasing dyspnoea on exertion, wheezing respiration, and a productive cough, and was unable to work. After a second febrile illness he was admitted to hospital in November, 1950.

He was severely ill and febrile, dyspnoeic, and cyanosed; there was no clubbing. Rhonchi and basal rales were widespread. The spleen, liver, and lymph nodes were not enlarged. He had 10–15 oz. (280–420 ml.) of thin mucoid sputum daily, which on culture yielded a mixed growth of organisms; numerous smears and cultures for *Mycobacterium tuberculosis* were negative. A chest radiograph showed patchy consolidation in the right middle and both lower zones. The tuberculin test was negative at 1/10 O.T. (1,000 T.U.). He was treated with penicillin and triple sulphonamides, but responded slowly. Bronchoscopy showed generalized inflammation of the whole bronchial tree, without ulceration of the mucosa. There was slit-like narrowing of the right upper lobe bronchus.

A biopsy specimen (Fig. 1) from the lower part of the right main bronchus showed multiple discrete epithelioid follicles, with fairly numerous giant cells, one of which contained a typical asteroid inclusion body. There was minimal necrosis of some of the follicles, but no caseation. He was treated as a case of tuberculous bronchitis, with streptomycin, 1 g., and sodium *para*-aminosalicylate (P.A.S.), 15 g. daily. After six weeks on this treatment there was no clinical improvement. Bronchoscopy on two further occasions (December, 1950, and January, 1951) showed, in addition to the stenosis of the right upper lobe bronchus, considerable narrowing of the left upper lobe bronchus and its divisions. During his stay in hospital his general condition and attacks of bronchospasm showed little change, but the sputum volume fell to approximately 5 oz. (140 ml.) daily.

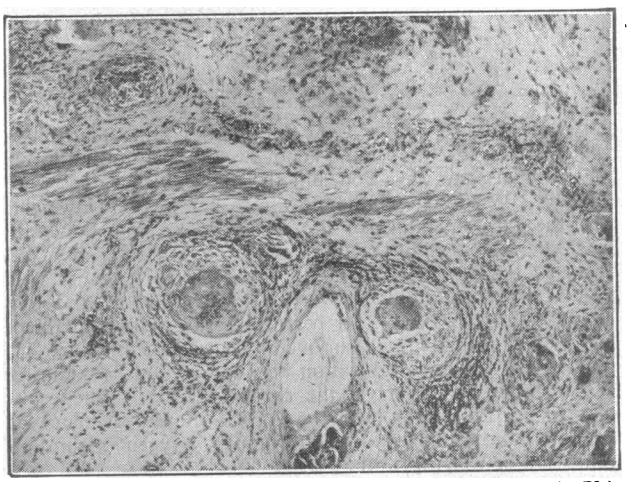

FIG. 1.—Case 1. Bronchial biopsy in December, 1950. (×70.)

He was discharged home in May, 1951, but the symptoms persisted and he was unable to work. There were several short febrile illnesses, responding to treatment at home. Chest radiographs showed soft opacities in all zones, especially in a contracted right upper lobe. After a course of rehabilitation in 1954 he resumed work in 1955 after six years' unemployment.

The improvement did not last, and, following an increase in his dyspnoea, he was readmitted to hospital in June, 1955. His physical signs were unchanged and a chest radiograph (Fig. 2) showed patchy clouding in the right upper lobe, at the right base, and in the left costophrenic angle. Bronchoscopy showed the slit-like stenosis of the right upper lobe bronchus to be unaltered; the lower part of the right main bronchus and the right lower lobe bronchus were irregular and distorted and mucopurulent secretion was excessive. A bronchogram showed marked stenosis of the right upper lobe, main (lower part), lower lobe, and apical lower bronchi; the anterior and posterior segments of the upper lobe failed to fill and there was poor peripheral filling in the lower lobe. On the left side there were stenoses of the upper division of the upper lobe bronchus and of the superior lingular bronchus, and poor peripheral filling in the upper lobe. There was irregular narrowing and dilatation of the smaller bronchi of both lungs. The tuberculin test was again negative to 1,000 T.U. Serum proteins, liver biopsy, and radiographs of hands and feet were normal. Treatment was started with cortisone, 100 mg., streptomycin, 1 g., and isoniazid, 300 mg., daily. The amount of sputum, which became mucoid, was greatly decreased and the

rhonchi were diminished in all areas. His dyspnoea decreased and the vital capacity rose from 2,700 to 3,800 ml. Cortisone was reduced to a maintenance dose of 50 mg. daily and he was discharged after three months in hospital.

The improvement was not maintained, but an increase in cortisone dosage to 75 mg. daily was effective. Later he again deteriorated; the treatment was temporarily stopped and he was readmitted in December, 1955. Treatment was started again and the dose of cortisone was increased to 175 mg. daily. A fifth bronchoscopy showed that the only part of the right bronchial tree which was not grossly stenosed was the right middle lobe bronchus. The left bronchial tree was less affected, with severe stenosis of the upper division of the upper lobe bronchus, and slight stenosis of the lingular bronchus. He improved on the increased dose of cortisone, but on reducing this to 100 mg. daily his symptoms recurred. Prednisone, 25 mg. daily, was gradually substituted, while continuing with streptomycin, 1 g. thrice weekly, and isoniazid, 400 mg. daily. In addition, 60 units of corticotrophin gel was given once weekly. On discharge in March, 1956, he had again improved, being able to walk upstairs without distress and producing only 1–2 oz. (28–56 ml.) of mucoid sputum. There were only occasional rhonchi.

Since discharge he has been well, and working, apart from one slight exacerbation requiring a temporary increase in the dose of prednisone. A chest radiograph in November, 1956, showed that great clearing had taken place in the right upper lobe, though the horizontal fissure was still raised; the lower zones were clear. Bronchoscopy in January, 1957, showed no significant change in the appearances of the major bronchi on the right side; on the left there was now slight narrowing of the main and lower lobe bronchi, in addition to stenosis of both divisions of the upper lobe bronchus.

Case 2

A housewife aged 53 was admitted to Brompton Hospital in April, 1956. In January, 1950, she had had a febrile illness with productive cough and dyspnoea, which was treated with penicillin. During the subsequent six years she had eight further similar attacks (the last in April, 1956), each of which was treated with a long course of an antibiotic. Between these episodes she had a spasmodic cough, with a trace of mucoid sputum, increasing dyspnoea on exertion, and "wheezing." Antispasmodic inhalations gave little relief and by 1956 she was breathless on very slight exertion.

On admission she looked ill but was afebrile. There was loud stridor, mainly inspiratory, clearly audible from the foot of the bed. The fingers were not clubbed. The heart was displaced to the right; the percussion note was impaired over the front of the right chest and the breath sounds were weak. A few rales were heard at the right apex, but no rhonchi; inspiratory stridor was widely audible. There was no enlargement of spleen, liver, or lymph nodes. A chest radiograph (Fig. 3) showed peaking of the right dome of the diaphragm and displacement of the heart and trachea to the right. There were homogeneous opacities in the right middle zone and at the right base. Some small circular shadows were seen at the right apex and in the right subclavicular region, and a few at the left apex. Hilar node enlargement was not apparent. Posterior view and lateral tomographs of the right lung showed a homogeneous opacity, probably pleural, situated anteriorly, a shrunken upper lobe, and bullae and honeycomb shadowing in the apical lower segment. A right bronchogram (Fig. 4) showed gross narrowing of the upper lobe bronchus, distortion of the main bronchus (lower part) and lower lobe bronchus, and gross narrowing of the latter; there was pointed occlusion of the middle lobe bronchus at its origin. There was considerable stenosis of the left main, upper, and lower lobe bronchi.

Bronchoscopy showed that the trachea was slightly compressed. The right main bronchus was displaced laterally and upwards and no trace of the right upper lobe bronchus could be found. Below this, the lumen narrowed rapidly and the middle and lower lobe orifices were seen as small slits; the rigidity of the bronchial tree was extreme. The left main bronchus was displaced upwards, so that an adequate view could not be obtained, but the lower lobe orifice could just be seen and was grossly stenosed. The mucosa everywhere appeared normal. Biopsy (Fig. 5) (from the carina between the middle and lower lobe bronchi) showed squamous metaplasia of the bronchial epithelium; there was one epithelioid follicle with several giant cells, no necrosis or caseation, but much acellular hyaline material. The tuberculin test was negative to 100 T.U. of P.P.D. Sputum culture yielded no pathogens; three specimens and one bronchoscopic trap specimen yielded no *M. tuberculosis* on smear or culture. Serum proteins and liver biopsy were normal.

After admission there was considerable clearing of the basal shadowing, attributed to reabsorption of pleural fluid; the upper zone was unchanged. Loud stridor and severe

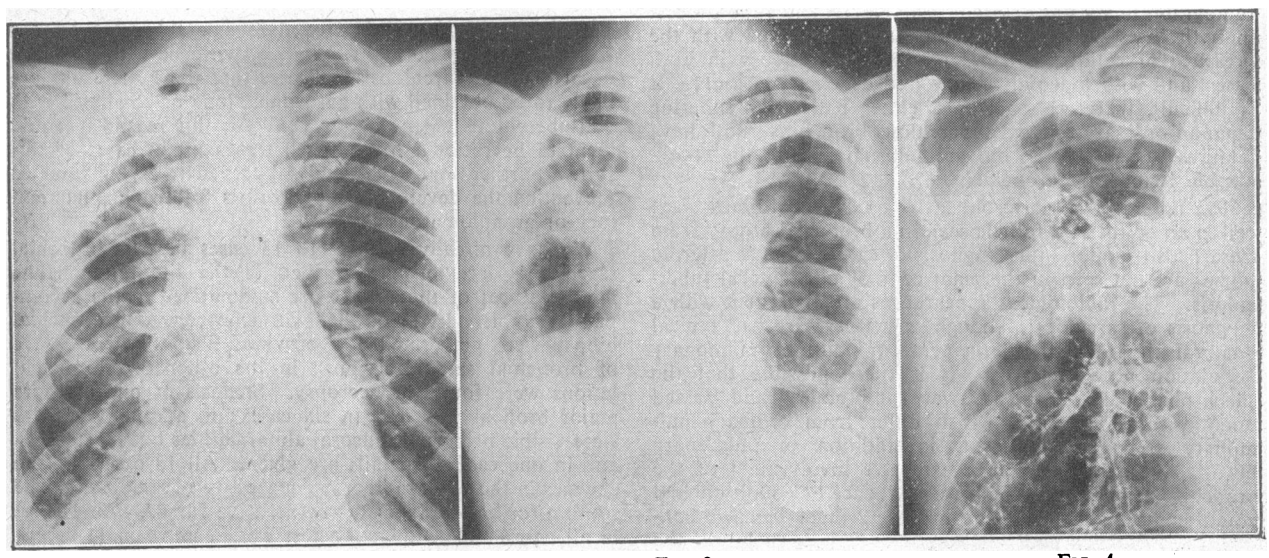

FIG. 2 FIG. 3 FIG. 4

FIG. 2.—Case 1. Chest radiograph (June, 1955) before treatment. FIG. 3.—Case 2. Chest radiograph, April, 1956.
FIG. 4.—Case 2. Right bronchogram, May, 1956.

dyspnoea persisted. Treatment was begun with streptomycin, 1 g., isoniazid, 200 mg., and prednisone, 40 mg., daily. One month later the dyspnoea was much less and the stridor barely audible. The vital capacity rose from 1,590 ml. to 2,760 ml. and the maximum breathing capacity from 14 to 31 l./min. Streptomycin was then discontinued and P.A.S. (12 g. daily) started. She was discharged and treatment with P.A.S. and isoniazid continued; the dose of prednisone was reduced to 20 mg. daily.

Improvement continued steadily; a radiograph in November, 1956, showed great clearing of the opacities, but

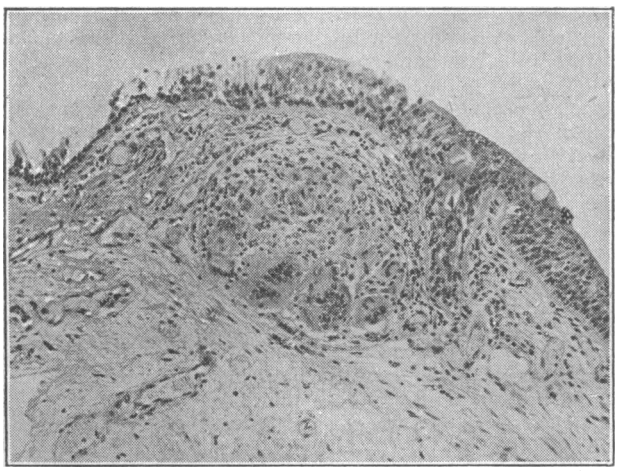

FIG. 5.—Case 2. Bronchial biopsy in May, 1956. (×125.)

persisting contraction of the right upper lobe with elevation of the right hilum. Bronchoscopy in January, 1957, showed that, though there was still gross narrowing of the right middle and lower lobe bronchi, this was less severe than previously; the right upper lobe orifice could now be seen, though the bronchus narrowed rapidly; a satisfactory view of the left side was not obtained. The improvement in the maximum breathing capacity was maintained (32.2 l./min.).

Discussion

These two cases were found to have multiple bronchostenoses, and bronchoscopic biopsy showed discrete non-caseating epithelioid follicles. The sputum contained no tubercle bacilli, the tuberculin test was negative (to 100 or 1,000 T.U.), and there were no pulmonary lesions on the radiograph to suggest tuberculosis. Nevertheless the process in both cases was clearly active, being associated with the presence of cellular follicles on bronchial biopsy in both cases, and with mucosal redness and oedema in Case 1. It is difficult, therefore, to regard either patient as suffering from an ordinary form of tuberculous bronchitis; both have features of sarcoidosis, but are unusual in that the recognizable lesions are bronchial.

The finding of an asteroid inclusion body within a giant cell in an epithelioid follicle seen in a bronchial biopsy from Case 1 also supports the diagnosis of sarcoidosis, as asteroid bodies are not seen in the giant cells of unequivocal tuberculosis. The radiological appearances are consistent with a diagnosis of sarcoidosis, though in neither case had typical bilateral hilar-node enlargement or diffuse pulmonary nodulation been observed. It is quite possible that the early phase of the disease was symptomless and passed unnoticed in our cases, which differ from ordinary pulmonary sarcoidosis in that, in addition to pulmonary fibrosis, there has also been extensive involvement of the bronchi. In both cases there was evidence of endobronchial granulomata and fibrosis, and in Case 2 there was also considerable distortion and rigidity of the main branches of the bronchial tree, as observed bronchoscopically. Bronchography confirmed the widespread distribution of the bronchial lesions, but bronchoscopic biopsy was crucial in suggesting the diagnosis.

The clinical features of these two cases are stridor, recurrent episodes of bronchopulmonary infection, and dyspnoea. In Case 2 stridor was very striking indeed. Before admission, however, this had been regarded as a wheeze indicative of asthmatic bronchospasm. In Case 1 stridor was inconspicuous, being concealed much of the time by wheezing from spasm and the presence of bronchial mucus. However, during treatment with prednisone the stridor was quite evident. Both patients gave histories of recurrent bronchopulmonary infections and both were seen during such an episode. These are to be attributed to infection of lung segments distal to partially occluded bronchi. Though these episodes responded to antibiotics, they did so slowly. Dyspnoea results from the development of large areas of virtually functionless lung and the additional respiratory work required to force air through constricted bronchi.

Both cases were treated with a combination of cortisone (or prednisone or corticotrophin) and antituberculous drugs. Many physicians employ such treatment in cases of sarcoidosis (Hoyle *et al.*, 1955) because of the commonly held belief in this country that many cases of clinical sarcoidosis are the unusual and atypical result of tuberculous infection; furthermore, active sputum-positive tuberculosis is not an uncommon complication of sarcoidosis, whether or not there is any causal relationship between tuberculous infection and sarcoidosis. Both cases responded to this treatment. In Case 1 the main benefit consisted in the relief of bronchospasm, the diminution in the volume of sputum, and the reduction in the number of infective episodes. In Case 2 there was a remarkable improvement in the dyspnoea and stridor, and this was borne out by the results of lung-function tests; there have been no further infective episodes. In both cases considerable radiological improvement occurred, though in neither has the radiograph returned to normal. Disappointingly, there has been little change in the bronchoscopic appearances, Case 1 being slightly worse and Case 2 rather better.

Treatment has been continued for only 18 months in Case 1 and for seven months in Case 2; it is therefore too early to say with confidence that the improvement will be maintained or whether treatment will have to be maintained indefinitely. It is impossible to state with certainty to which of the therapeutic agents the improvement is to be attributed. However, in Case 1 a course of streptomycin and P.A.S. alone (admittedly a short course, lasting only six weeks) was without effect, and an attempt to reduce the dose of cortisone below 125 mg. was followed by deterioration. In Case 2 no such evidence exists. Three of the reported cases of bronchial sarcoidosis (Siltzbach and Som, 1952; Turiaf and Brun, 1955) improved considerably when treated with cortisone or corticotrophin. Experience with the more usual types of sarcoidosis indicates that the best results are likely to be obtained with cortisone, alone or combined with antituberculous chemotherapy, and for this reason it would seem to be rational to use such treatment in cases of this sort. Furthermore, cortisone is believed to be of value in preventing the development of fibrosis following inflammatory or granulomatous lesions.

We have already referred to 13 cases of true bronchial sarcoidosis, previously described in the literature. The main features of these cases are summarized in the accompanying table. In 11 of them bronchoscopy and bronchial biopsy were performed and provided histological evidence of bronchial sarcoid lesions; in the other two bronchial lesions were found at necropsy. Stenosis of one or more major bronchi was seen in six cases; in another six there were visible bronchial mucosal abnormalities but no stenosis, and in one case no details are given. All 13 cases showed changes in the chest radiograph suggestive of sarcoidosis. The sputum (or gastric lavage) was negative for *M. tuberculosis* in all cases. The tuberculin test was negative in 11 cases; in one it was positive at 1 in 100, and in another weak positive to 10 T.U. (1 in 1,000). In seven cases the diagnosis was confirmed during life by other histological evidence (biopsy of subcutaneous nodule in two and lymph-node

Cases of Bronchial Sarcoidosis

Authors	Age and Sex	Hilar Lymph Nodes	Pulmonary Changes	Clinical Features and Extrathoracic Lesions	Sputum for *M. tub.* (or Gastric Lavage)	Tuberculin Test	Other Investigations	Bronchoscopy and Biopsy	Treatment and Progress
Benedict and Castleman (1941)	20 F	+	Lung fields clear	Cough, night sweats, loss of weight. Fever, generalized lymph-node enlargement, subcutaneous nodules. Respiratory difficulty suggestive of partial tracheal or bronchial obstruction	–	– (1/100)	Biopsy of skin nodule and lymph node showed sarcoid	Narrowing of both main bronchi; yellowish "bleb-like lesions" (2–3 mm.). Biopsy: many non-caseating epithelioid cell follicles with giant cells	No active treatment. Spontaneous clinical improvement
Olsen (1946) ..	47 M	+	Extensive infiltration in R. lung and L.U.Z.	Cough, hoarseness, dysphagia. Cranial nerve palsies (IX and X)	–	– (1st and 2nd strengths)		Nodular appearance of lateral wall of R. main bronchus. No stenosis. Biopsy non-caseating epithelioid cell follicles	Gold treatment with little benefit. Later spontaneous clinical and radiological improvement
Jacobs (1949) ..	26 M	+	Diffuse nodular foci through both lung fields	Dry cough. Enlarged axillary and cervical lymph nodes. Bone lesions	– (G.L.)	– (1 mg.)	Lymph-node biopsy: sarcoid. Increased β- and γ-globulin. Decalcification and reticulation of two phalanges	Lateral compression of L. main bronchus. Red haemorrhagic areas (2–3 mm.) in region of R. "first dorsal" bronchus. Biopsy: non-caseating epithelioid cell follicles with giant cells surrounded by collagenous sclerosis	Streptomycin ineffective. Later regression of hilar nodes, but pulmonary lesions increased
Vogt (1949) ..	58 F	+	Diffuse nodular and streaky opacities. Pleural thickening. Bullous emphysema. Recurrent bronchopneumonia	Progressive cough, dyspnoea. Fever, rigid chest with prolonged expiration, generalized lymph-node enlargement, skin lesions, hepatosplenomegaly, pericardial and ?cardiac lesions with partial heart-block	–	–	Biopsy of skin nodule: sarcoid. Increased serum globulin	Necropsy: bronchial mucosa dark red and injected; no stenosis. Histology: numerous epithelioid cell follicles with giant cells and calcareous inclusion bodies	Progressive deterioration. Died
Siltzbach and Som (1952)	40 M	+	Shrinkage and consolidation of R.M.L. Faint linear and nodular opacities through both lung fields	Cough and purulent sputum, night sweats, loss of weight, wheezing. Fever, generalized lymph-node enlargement, splenomegaly, quiescent uveitis	–	– (1/100)	Lymph-node biopsy: sarcoid. Kveim test +. Increased serum globulin. Bronchiectasis R.M.L.	Stenosis of R. middle lobe bronchus with granular thickened mucosa. Biopsy: non-caseating epithelioid cell follicles with giant cells and surrounding inflammatory cells	Antibiotics ineffective. Cortisone produced great clinical, radiological, and bronchoscopic improvement
" "	35 F	+	Linear opacities R.L.Z.	Cough, dyspnoea, wheezing. Stridor, prolonged expiration, and rhonchi. Enlarged axillary lymph nodes	–	– (1/100)		Narrowing of L. main bronchus and lower part of R. main bronchus; mucosa of R.M.L. bronchus thickened with narrowing of lumen. Biopsy: numerous non-caseating epithelioid cell follicles with giant cells with Schaumann bodies	No active treatment. Gradual spontaneous clinical and radiological improvement
Turiaf and Brun (1955) Case 1 (also Brun and Viallier, 1948, 1950)	39 M	–	Dense infiltration in both mid-zones with bullae	Recurrent febrile episodes with productive cough. Signs of diffuse bronchitis and emphysema, enlarged epitrochlear lymph node. Hepatic lesions (necropsy)	–	–	Lymph-node biopsy: sarcoid	Necropsy: large bronchi invaded by granulomatous tissue with epithelioid cell follicles and giant cells. Bronchioles surrounded, narrowed, and elongated	Steady downhill course to death. Terminal right spontaneous pneumothorax
Turiaf and Brun (1955) Case 2 (also Harvier *et al.*, 1950; Turiaf *et al.*, 1952, 1953)	34 F	+	Segmental opacity of right medial basal segment. Bilateral miliary opacities	Cough, dyspnoea, wheezing. Enlarged cervical lymph nodes, toxic goitre. Later fever, splenomegaly, right spontaneous pneumothorax	–	– (3 mg.) later +	Lymph-node biopsy: sarcoid B.M.R. +34%	Mucosa of both main bronchi reddened and thickened. Slit-like narrowing of R. main bronchus. Biopsy: non-caseating epithelioid cell follicles with giant cells	Streptomycin ineffective. Later spontaneous clinical, radiological, and bronchoscopic improvement and final complete return to normal
Turiaf and Brun (1955) Case 3 (also Turiaf *et al.*, 1952, 1953)	25 M	+	Soft infiltration on left and slight reticulation on right	Productive cough, loss of weight, weakness, sweats. Fever, enlarged axillary and epitrochlear lymph nodes	– (G.L.)	– (50 T.U.)	Lymph-node biopsy: sarcoid	Inflammation of L. bronchial tree with irregularity of lip of L. upper lobe orifice. Biopsy: non-caseating epithelioid cell follicles with giant cells and inflammatory cells	Clinical improvement, but persisting radiological abnormality in L.M.Z.
Turiaf and Brun (1955) Case 4 (also Turiaf *et al.*, 1952, 1953)	28 M	+	Infiltration at R. base and later diffuse nodular lesions through both lung fields	Polyarthritis and erythema nodosum. Fever, weakness, loss of weight. Splenomegaly	– (also G.L. –)	+ (1/100)		Thickened mucosa at lip of R. upper lobe orifice and of L. lower lobe bronchus. Biopsy: non-caseating epithelioid cell follicles with giant cells. Oedema and inflammatory cells	Progressed in spite of treatment with isoniazid
Turiaf and Brun (1955) Case 5	52 F	–	Diffuse bilateral nodulation	Dyspnoea. No further clinical details	–	–	Increased serum globulin	Bronchoscopic appearances not described. Biopsy: non-caseating epithelioid cell follicles with giant cells	No details given
Turiaf and Brun (1955) Case 6 (also Turiaf *et al.*, 1952, 1953)	41 M	+	Thickened horizontal fissure and opacity in right costophrenic angle	Pleurisy at 13 years. Pericarditis at 36. Recurrent pulmonary infections with pleurisy and arthralgia. Dyspnoea. Fever, salivary gland enlargement, iridocyclitis	–	Weak + (1/10)		Slight thickening and reddening of mucosa of R. bronchial tree, especially middle-lobe bronchus. Biopsy: numerous non-caseating epithelioid cell follicles. No giant cells	Treatment with corticotrophin and cortisone followed by clinical recovery and radiological improvement
Turiaf and Brun (1955) Case 7 (also Turiaf *et al.*, 1952, 1953)	58 F	+	Diffuse pulmonary opacities and reticulation	Dyspnoea, wheezing, and productive cough. Salivary gland enlargement, iridocyclitis, slight enlargement of lymph nodes, splenomegaly	–	– (1/100)		Reddening of mucosa of both main bronchi and mucosal thickening of lip of R. upper lobe bronchus, lower part of R. main bronchus and L. upper lobe bronchus, which is grossly narrowed. Biopsy: numerous non-caseating epithelioid cell follicles	Progressive deterioration followed by clinical and radiological improvement on cortisone

Longcope and Freiman (1952) and Cowdell (1954) each refer to one patient in whom the diagnosis of sarcoidosis was made by bronchoscopic biopsy, but give no further details. Turiaf and Brun (1955) refer to seven positive bronchial biopsies, but give details of only six (Cases 2–7 in their monograph).

biopsy in six); in two of these the diagnosis was also confirmed at necropsy. Symptoms and signs of respiratory obstruction, notably stridor or wheezing suggestive of asthma, were recorded in six cases and definite episodes of bronchopulmonary infection in three; productive cough, dyspnoea, and fever occurred in almost all. Improvement following treatment with cortisone or corticotrophin occurred in the three cases in which these agents were used.

Turiaf and Brun (1955) devote a chapter in their monograph on sarcoidosis to the discussion of bronchial involvement and the bronchoscopic findings. After considering extrinsic compression of bronchi by enlarged hilar glands, which is exceptionally rare, Turiaf and Brun proceed to discuss true bronchial sarcoidosis. This may take the form of granulomatous infiltration or of cicatricial stenosis, sometimes with resulting atelectasis, obstructive emphysema, retention and infection of secretions, or bronchiectasis. However, such sequelae are unusual (in contradistinction to tuberculosis) and bronchial sarcoidosis is commonly silent. They state that bronchial lesions are inconstant in the early stages of pulmonary and hilar glandular sarcoidosis, though they do often occur in active cases with fever and visceral manifestations. In such cases these are commonly unassociated with any clinical evidence of bronchial involvement. But in the late ("bullous-emphysematous" and "dense infiltrative") forms of the disease bronchial involvement is invariably present.

They point out that, since bronchial sarcoidosis can occur in the absence of specific symptoms or signs, bronchoscopy and bronchial biopsy are important in the recognition of bronchial involvement. They have seen 15 cases with bronchoscopic abnormalities. In only two was the mucosa grossly abnormal, but in 11 it was inflamed, though the appearances were not distinctive. Stenosis is caused in some cases by warty granulations, and in others by cicatricial fibrosis. Associated with the mucosal inflammation, there may be excessive bronchial secretions, often secondarily infected. Bronchial biopsies were performed in these 15 cases, and in seven the histological examination showed indisputable microscopical sarcoids. They found that, though it is preferable to take the specimen from the parts of the bronchial mucosa which appear most abnormal, there may be typical epithelioid follicles even when the macroscopic changes are inconspicuous.

Cowdell (1954) states: "We have once made a presumptive diagnosis on bronchoscopic biopsy, later confirmed when lymph-node enlargement appeared," but gives no further information about this case. He comments, however, that a biopsy in sarcoidosis should provide a reasonably large portion of tissue, as a small specimen (for example, from needle biopsy of the liver) "may contain only one or very few granulomata and may consequently be insufficient to show the general uniformity of pattern which is one of the most important features."

It is clear that in cases of undoubted sarcoidosis with lesions in well-recognized situations and with histological confirmation, bronchial involvement may occur; this may be associated with the presence of neighbouring hilar-node enlargement and extrinsic bronchial compression, but, on the other hand, the bronchial wall may be affected primarily. Mucosal abnormalities are recognized and stenosis is common.

From this account it can be seen that our cases were similar in their pulmonary and bronchial manifestations to those previously reported cases of sarcoidosis with bronchial involvement. A striking feature, however, is that, whereas these cases usually have had extrathoracic sarcoid lesions, in our cases there were no such manifestations or biochemical abnormalities, and liver biopsy was negative.

Citron (1955) has described a case in many ways similar to our cases under the title of "Multiple tuberculous bronchial stenosis." A man aged 31, with a past history of tuberculous cervical nodes, had recurrent febrile bronchopulmonary infections with pulmonary opacities on the radiograph; there were stridor and generalized rhonchi. Bronchography and bronchoscopy showed multiple stenoses of bronchi, and a bronchoscopic biopsy showed "typical tubercles with little caseation." Numerous specimens of sputum yielded no *M. tuberculosis* on culture, but the tuberculin test was positive to 10 T.U. of P.P.D. This patient improved on treatment with cortisone and antituberculous drugs. No reference is made to any extrathoracic manifestations of the disease.

Summary and Conclusions

Two cases are reported in which multiple bronchial stenoses were associated with a negative tuberculin test and negative sputum; bronchial biopsy revealed non-caseating epithelioid follicles. We regard these as examples of sarcoidosis, predominantly affecting the bronchi.

The main clinical features in our cases were recurrent bronchopulmonary infections, stridor, and progressive dyspnoea. Extrathoracic manifestations of sarcoidosis were absent. The occurrence of these symptoms without adequate explanation calls for bronchoscopy and bronchial biopsy; bronchography may also give useful information.

Preliminary experience suggests that steroid therapy may be helpful, and it is probably wise to combine this with antituberculous chemotherapy.

Bronchial lesions do occur in sarcoidosis, but have hitherto been given little attention in the literature. Thirteen reported cases are reviewed.

We thank Dr. J. L. Livingstone and Dr. N. C. Oswald for permission to publish these cases and for valuable advice during the preparation of this article. We also acknowledge our debt to Dr. J. G. Scadding for drawing our attention to the occurrence of cases of this sort, and to Dr. G. Simon for advice on the radiological interpretation.

ADDENDUM.—Since this article was prepared, Citron and Scadding (*Thorax*, 1957, **12**, 10) have reported three cases—one of which is quoted above (Citron, 1955)—closely resembling ours; in one the tuberculin test was positive (to 100 T.U.) and in another the sputum was found on two occasions to contain acid-fast bacilli. They regard their cases as having sarcoidosis of the bronchi, but think that they are all of tuberculous aetiology. Kalbian (*Thorax*, 1957, **12**, 18) describes the bronchoscopic appearances in 11 consecutive cases of pulmonary sarcoidosis (none of more than two years' duration); in four the appearances were virtually normal, in one the only abnormality was distortion of the carina, in five the mucosa was thickened or granular, and in one (Case 9) there was also stenosis of the right middle and lower lobe bronchi. In three cases bronchial biopsy showed non-caseating tubercles and in three others giant cells were seen.

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