

# Thoracic actinomycosis

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Six cases of pulmonary infection with *Actinomyces Israeli* and one case of infection with *Nocardia asteroides* are described. The incidence of thoracic actinomycosis has declined recently and the classical presentation with chronic discharging sinuses is now uncommon. The cases described illustrate some of the forms which the disease may take. Actinomycotic infection has been noted, not infrequently, to co-exist with bronchial carcinoma and a case illustrating this association is described. Sputum cytology as practised for the diagnosis of bronchial carcinoma has helped to identify the fungi in the sputum. Treatment is discussed, particularly the possible use of oral antibiotics rather than penicillin by injection.

Actinomycosis is not common in this country. The Table shows the number of cases reported to the Public Health Laboratory Service from public health and hospital laboratories in the United Kingdom and Republic of Ireland in recent years. It is usually considered that the chest may be involved in about 15% of cases (Cecil and Loeb, 1963). But, of the 36 cases reported in 1970, the chest was involved in only one case. In 1957 Bates and Cruickshank published an account of 85 cases of thoracic actinomycosis collected from many thoracic centres in this country. One of the co-authors of this paper (G. C.) was formerly senior surgeon of this unit. This series of cases is still widely regarded as giving the classical description of actinomycosis of the chest. Now, in addition to a reduced incidence, thoracic actinomycosis may have a different clinical presentation. Therefore, an account of a small recent series of cases may be of interest.

TABLE

INCIDENCE OF ACTINOMYCOSIS AS REPORTED FROM PUBLIC HEALTH SERVICE AND HOSPITAL LABORATORIES (Central Public Health Laboratory, Colindale)

	1966	1967	1968	1969	1970	Total
No. of cases	25	27	21	60	36	169

## CASE REPORTS

### ACTINOMYCOSIS

**CASE 1** J. S., a 42-year-old man was a commercial traveller and a heavy smoker. A febrile illness was followed by cough, weight loss, and lassitude but no pain. A chest radiograph (Fig. 1) showed shadowing in the region of the right lung hilum. On bronchoscopy the mucosa around the right upper lobe orifice was injected and swollen. Biopsy of this area

showed only submucosal fibrosis. Cytological examination of the sputum showed the presence of fungus (Figs 2 and 3) and cultures gave a growth of *Actinomyces Israeli*. The patient was hypersensitive to penicillin and was treated with oral tetracycline, 2 g daily for six months. There was marked reduction in the shadowing on the chest film after only six weeks of treatment (Fig. 4) and subsequently complete disappearance. The patient has remained well for six years.

**Comment** Carcinoma of the bronchus was originally strongly suspected but sputum cytology gave the clue to the diagnosis. Complete resolution was obtained with oral tetracycline.

**CASE 2** M. B., a 71-year-old housewife, had a six weeks' history of cough with shortness of breath on exertion. A chest radiograph (Fig. 5) showed an opacity at the hilum of the left lung. Sputum cytology showed the presence of ray fungus and subsequent sputum cultures gave a growth of *A. Israeli*. She was treated for one month with penicillin, 4 million units daily, by intramuscular injection and sulphamethazine, 4 g daily. After this she received tetracycline, 1 g daily for one month.

After treatment sputum cultures have been persistently negative for fungi and she has lost her cough. The chest film (Fig. 6) showed clearing of the left hilar shadowing and her condition has been satisfactory for the past three years.

**Comment** Bronchial carcinoma was thought to be the most likely diagnosis from the appearance of the chest films. Cytological examination of the sputum was important.

**CASE 3** B. C. was a 34-year-old housewife. At the age of 19 years, when a student nurse, she had developed fever and cough. A chest radiograph (Fig. 7) showed collapse of the middle lobe of the lung. *Mycobacterium tuberculosis* was not found in the sputum, but the condition was regarded on clini-

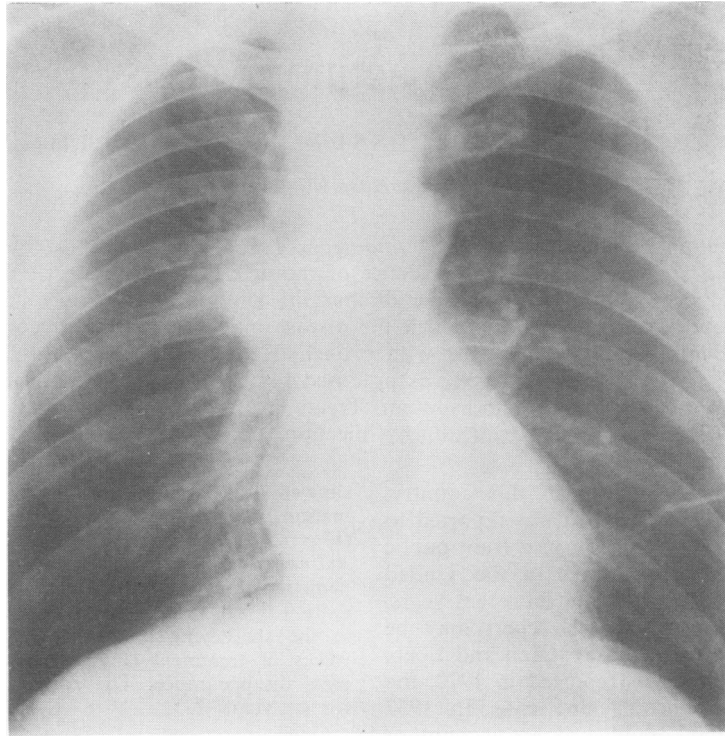


FIG. 1. Case 1. Initial chest film showing right hilar shadowing.

cal grounds as being due to tuberculosis. She was treated for three months with streptomycin, INAH, and PAS and for a further six months with INAH and PAS. After this time operation was performed, at another hospital, for resection of the middle lobe. Unfortunately, the histological report on the operation specimen is not available. However, the operation notes record that there was such dense fibrosis that identification of the hilar structures was almost impossible.

After the resection the patient remained well for almost one year and then developed recurrent episodes of fever with cough and purulent sputum. She was treated by numerous short courses of tetracycline or ampicillin. Sputum cultures were negative for tubercle bacilli and other pathogenic organisms. Chest films showed increased shadowing on the right side (Fig. 8). At bronchoscopy it was seen that the stump of the middle lobe bronchus was present and a bronchogram (Fig. 9) demonstrated that the opacity lay at the site of the middle lobe and showed a deformity of the anterior segmental bronchus of the upper lobe. A chronic abscess due to a fistula from the middle lobe stump was suspected and exploration was performed after a six weeks' course of PAS and INAH. The pleural cavity was completely obliterated by adhesions and there was dense

fibrosis around the hilum of the lung. There was an abscess cavity anteriorly between the upper and lower lobes of the lung. The anterior segment of the right upper lobe was solid and partially invaded by the abscess cavity. The abscess contained pus with typical 'sulphur granules'. Pus from the abscess grew *A. Israeli* on culture. No tubercle bacilli were found on culture or on guinea-pig inoculation. Segmental resection of the anterior segment of the right upper lobe was performed and as much as possible of the thick-walled abscess cavity was excised.

After operation the patient was treated with penicillin by intramuscular injection, 8 million units daily for three weeks and then 6 million units daily for 14 weeks. After this she received tetracycline, 2.0 g daily for 12 weeks. PAS and INAH were also given for the first eight months of the postoperative period. She has remained well over the past five years.

*Comment* This case illustrates the considerable technical difficulties of surgical treatment for pulmonary actinomycosis because of the dense adhesions. The ineffectiveness of antibiotics in intermittent and low dosage is well shown. Probably the condition was due entirely to actinomycosis but antituberculous treatment was also given because of the original diagnosis.

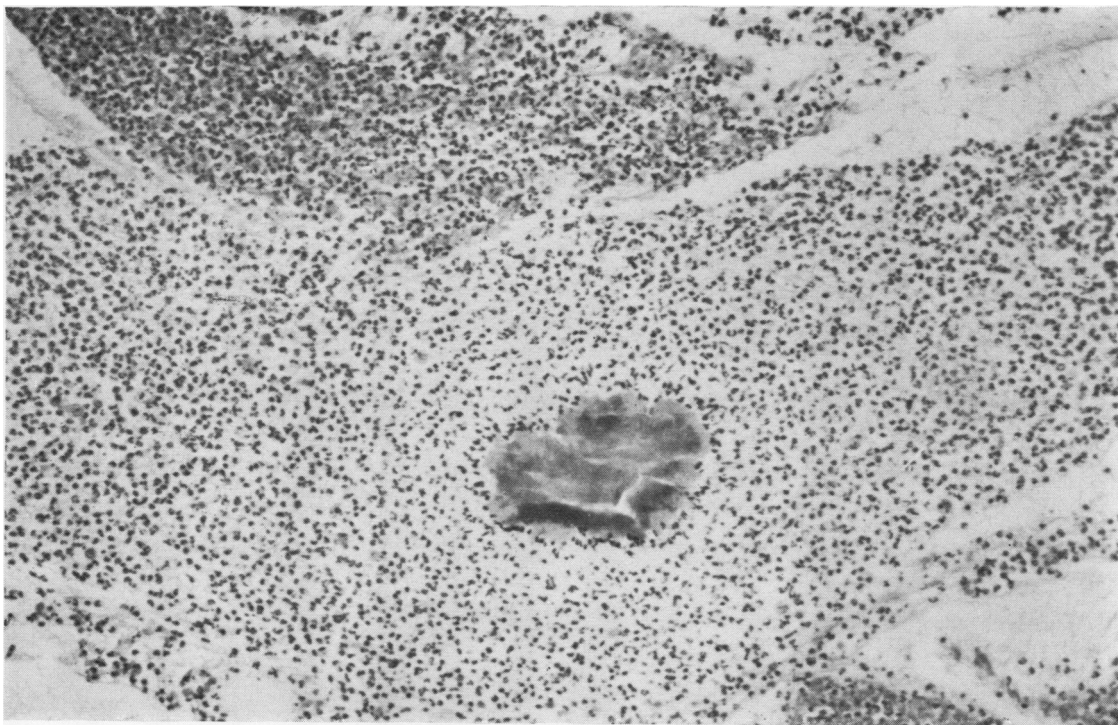


FIG. 2. *Case 1. Section of sputum showing fungus 'granule'. (H. and E.  $\times 80$ .)*

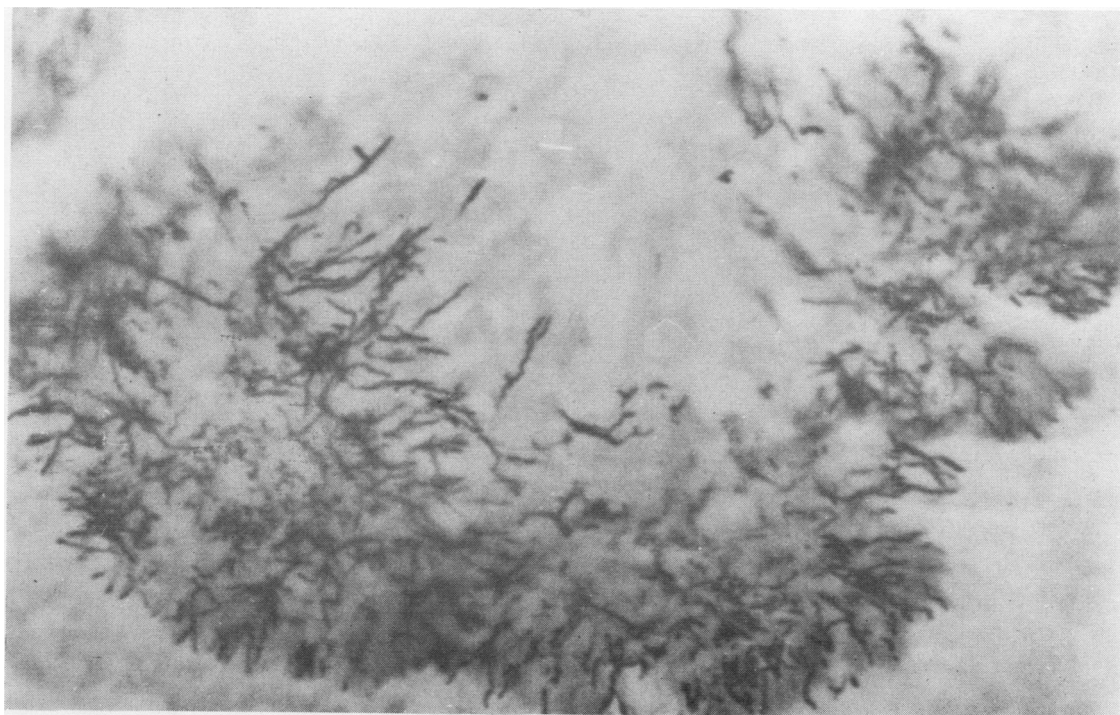
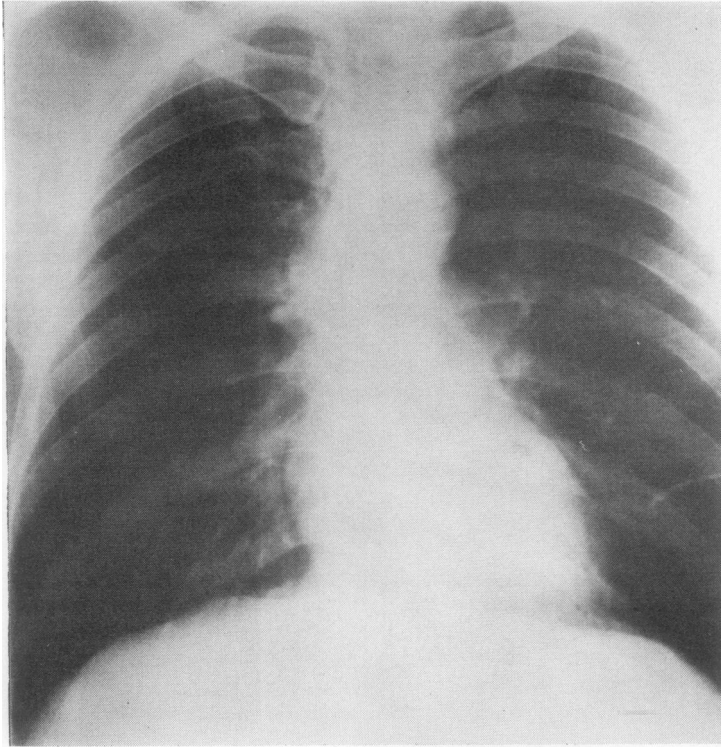
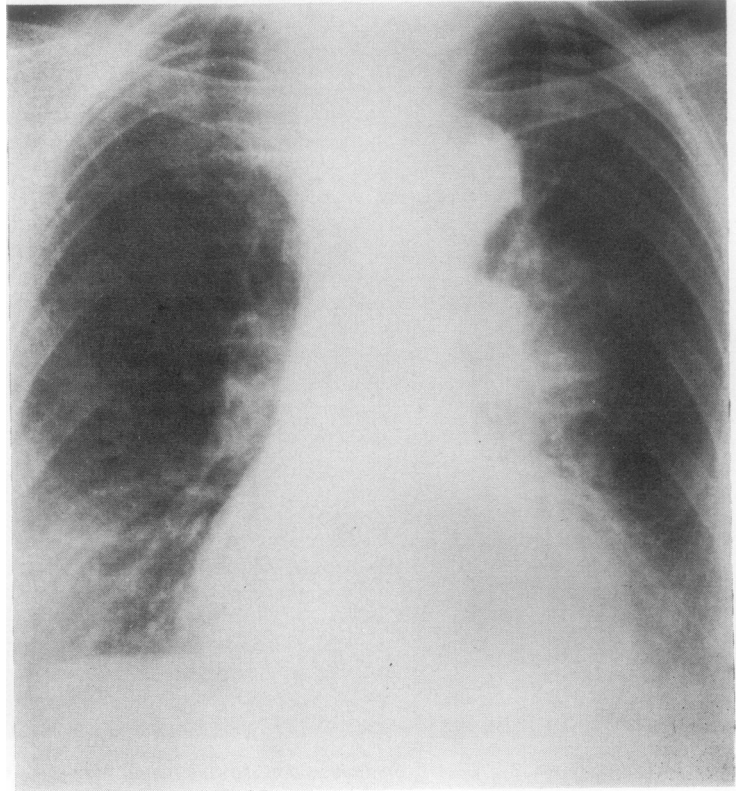


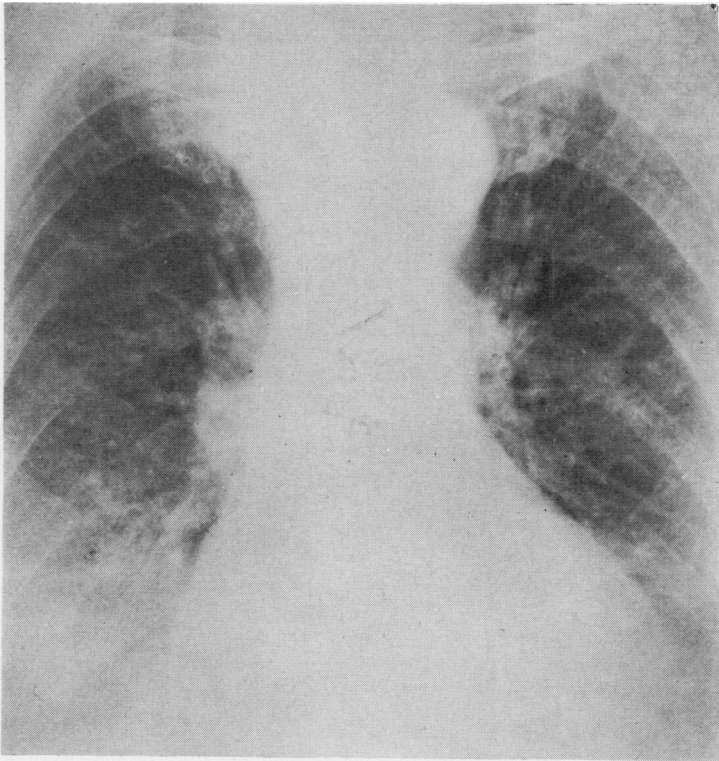
FIG. 3. *Case 1. Sputum section showing fungus filaments. (Gram stain  $\times 320$ .)*



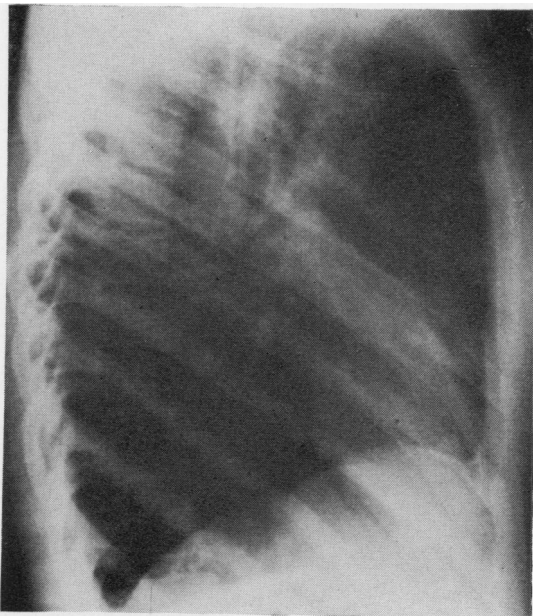
**FIG. 4.** *Case 1. Chest radiograph showing considerable diminution of shadowing after six weeks' treatment.*



**FIG. 5.** *Case 2. Initial chest film showing left hilar opacity.*



**FIG. 6.** *Case 2. Clearing of left hilar opacity after two months' treatment.*



**FIG. 7.** *Case 3. Initial chest film showing middle lobe collapse.*

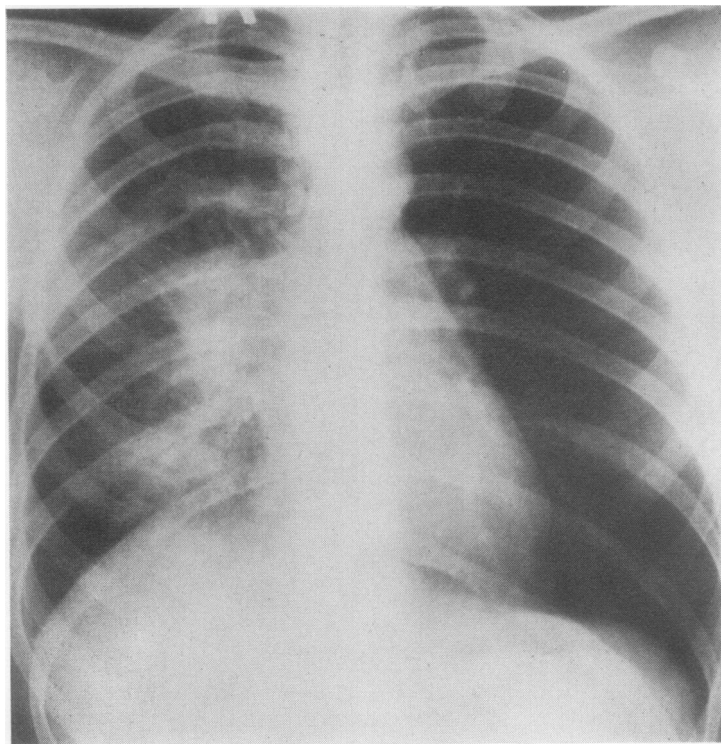


FIG. 8. *Case 3. Increased opacification on right side after middle lobectomy.*

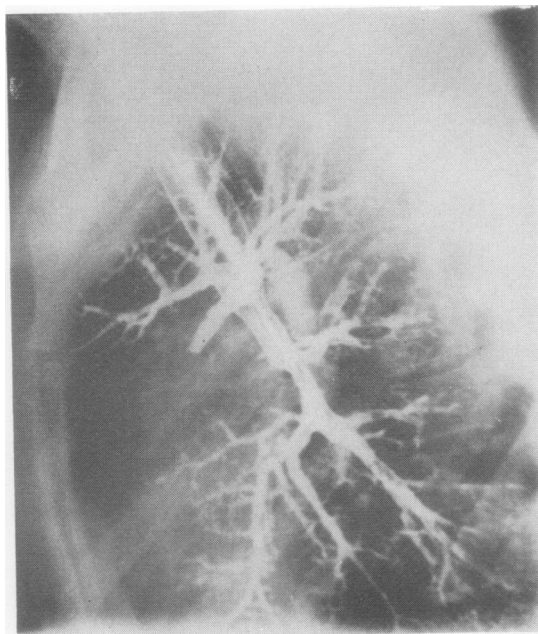


FIG. 9. *Case 3. Right lateral bronchogram.*

CASE 4 A. G., a 41-year-old housewife had a five months' history of episodes of fever associated with cough, purulent sputum, and occasional haemoptyses. A chest film (Fig. 10) showed consolidation in the area of the middle lobe and a bronchogram

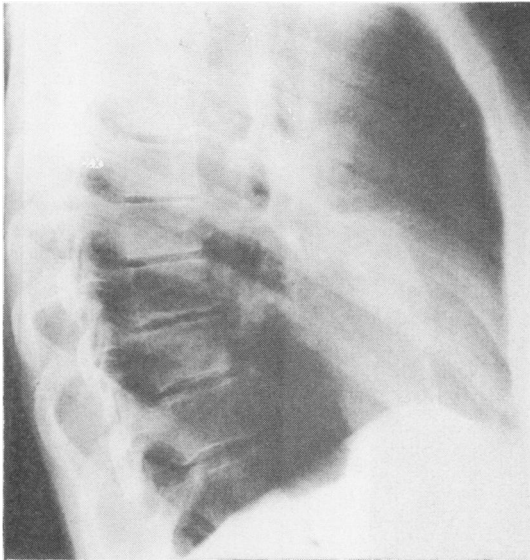


FIG. 10. Case 4. Right lateral film showing middle lobe collapse and consolidation.

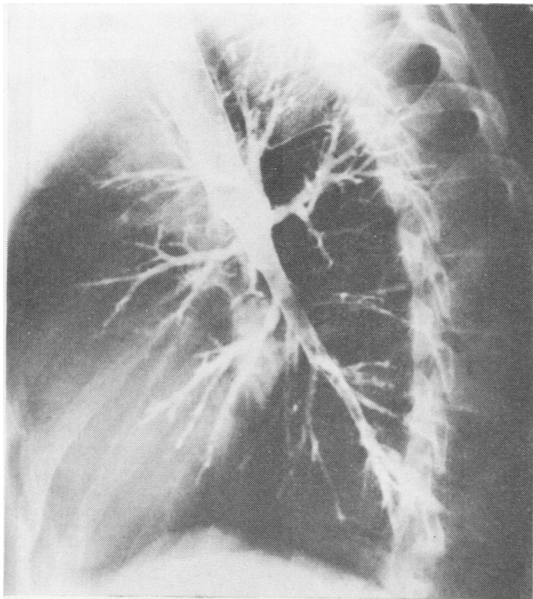


FIG. 11. Case 4. Right lateral bronchogram showing narrowing of proximal middle lobe bronchus.

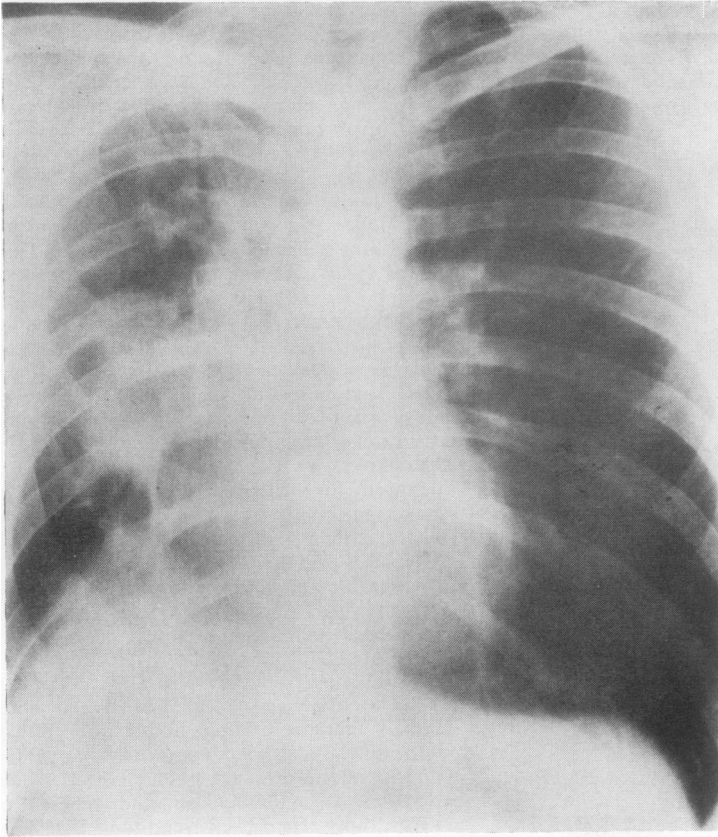
(Fig. 11) demonstrated stenosis of the origin of the middle lobe bronchus. No tubercle bacilli or other pathogenic organisms were found on sputum culture. The stenosis was considered to be most likely due to compression of the middle lobe bronchus by tuberculous lymph nodes.

Streptomycin, PAS, and INAH were given for six weeks and then a right thoracotomy was performed. The pleural cavity was obliterated by adhesions. The middle lobe was consolidated and there was very dense fibrosis around the lung hilum. There were calcified lymph nodes adherent to the root of the middle lobe bronchus in keeping with the diagnosis of Brock's syndrome (Brock, 1950). A middle lobectomy was performed. The operation specimen showed a large abscess cavity in the medial segment. Histological examination of the abscess wall showed inflammatory granulation tissue with fungus granules present. Culture of the pus grew *A. Israeli* but no tubercle bacilli were found on smear or culture. After operation the patient received penicillin by intramuscular injection, 8 million units daily for three weeks and then 6 million units daily for eight weeks. After this she had tetracycline, 2.0 g daily for four weeks. Postoperative antituberculosis cover was also given with PAS and INAH for six months. She has remained well over a period of five years since the operation.

*Comment* The presence of calcified lymph nodes makes it likely that the original middle lobe disease was due to tuberculosis. Actinomycosis has a tendency to occur in the presence of devitalized tissues. The association of actinomycosis and tuberculosis has, however, not often been reported. Bates and Cruickshank (1957) quote two cases and Lee (1966) gives details of one case.

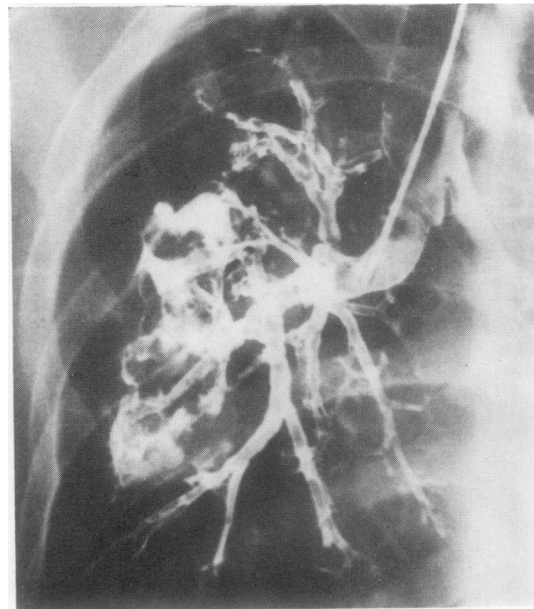
CASE 5 K. G., a 38-year-old sheet metal worker, attended this hospital with a history of wheezing, shortness of breath on exertion, and cough with purulent sputum of two years' duration. A chest radiograph and bronchogram showed an area of consolidation with cavitation in the right upper lobe of the lung. On bronchoscopy pus was seen coming from the right upper lobe orifice. Sputum cultures gave a growth of *Escherichia coli*. A right thoracotomy was done. There was such dense fibrosis around the lung hilum that great difficulty was encountered in dissecting the vessels and the middle lobe had to be removed as well as the upper lobe. Histological examination of the excised specimen showed a chronic abscess cavity with surrounding fibrosis.

About six months after this operation the patient again complained of bouts of fever and cough with purulent sputum. Over the next three years, chest radiographs (Fig. 12) showed increasing opacification of the right lung and a bronchogram (Fig. 13) showed the dye entering a large posterior intrapleural space from the lower lobe. At this time several specimens of sputum gave a growth of *A. Israeli* on culture.



**FIG. 12.** *Case 5. Chest radiograph three years after right upper and middle lobectomy showing increased shadowing on right side.*

**FIG. 13.** *Case 5. Right bronchogram showing large dye-filled intrapleural space.*





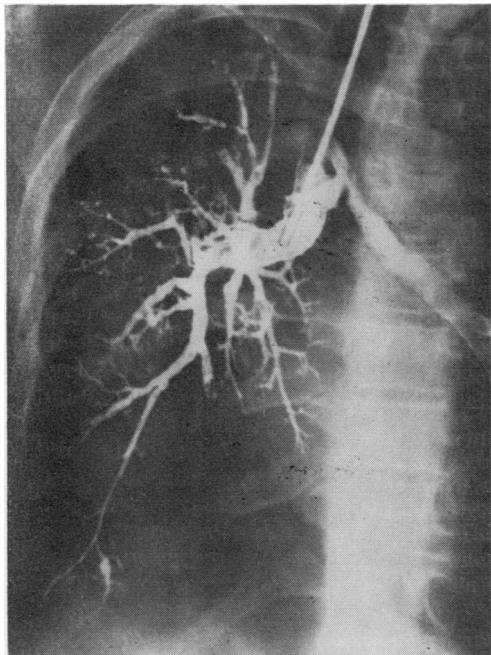


FIG. 14. Case 5. Right bronchogram after treatment.

The patient was treated with intramuscular penicillin, 6 million units daily, and sulphadiazine, 2 g daily for two weeks. Unfortunately, owing to an error, he then received only 600,000 units of penicillin once daily for a period of about five months. He continued to have a chronic cough with much purulent sputum. Sputum cultures continued to show a growth of *A. Israeli*. He was readmitted to hospital and given penicillin, 4 million units daily, by intravenous infusion for six weeks. This treatment was followed by tetracycline, 2 g daily for three months. Following this treatment he has become asymptomatic. A repeat bronchogram (Fig. 14) no longer shows the large dye-filled space. Sputum cultures have remained negative for *Actinomyces* over a period of three years.

*Comment* The fact that such dense fibrosis, which is a feature of actinomycotic infection, was encountered at the original operation, must make it likely that the condition was due to actinomycosis from the start. This case illustrates the necessity for high dosage and prolonged antibiotic treatment in chronic pulmonary actinomycosis.

CASE 6 F. M., a 40-year-old labourer, had first presented about 10 years previously complaining of pain in the right side of the chest. A chest radiograph (Fig. 15) showed a foreign body in the apical segment of the right lower lobe. The patient gave a

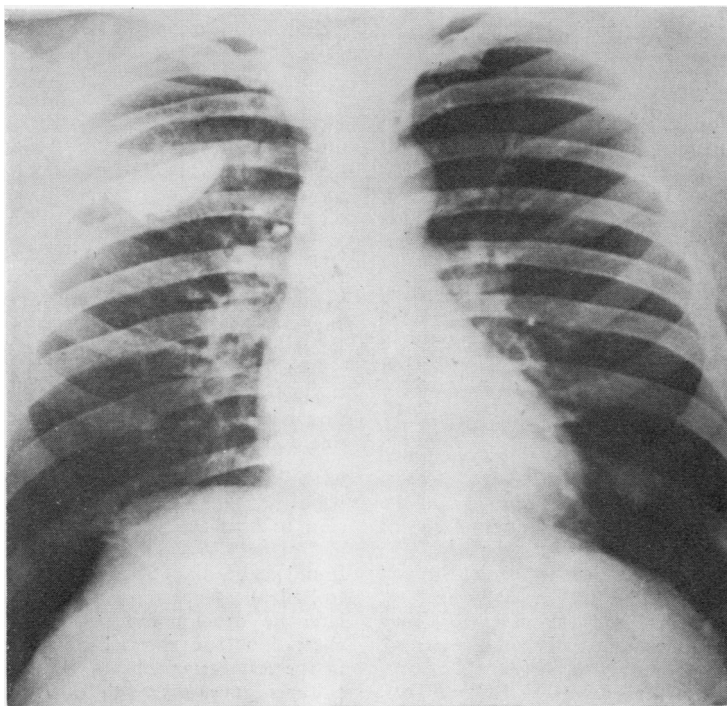


FIG. 15. Case 6. Portion of knife blade in right lung.

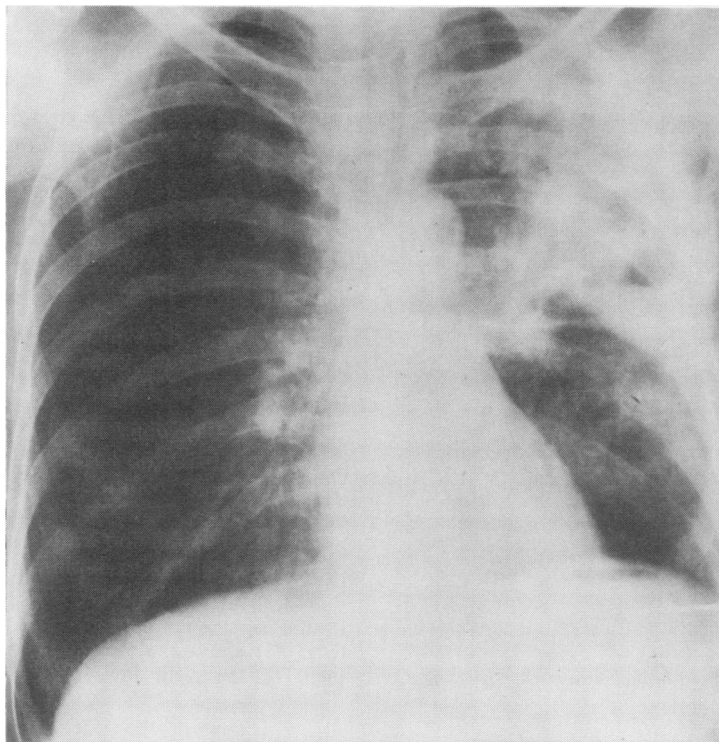


FIG. 16. Case 7. Chest radiograph at start of illness showing consolidation and cavitation in left upper lobe.

history of receiving a knife wound in the chest 20 years previously. Segmental resection of the apical and subapical segments of the right lower lobe and the contained piece of knife blade was performed. Histological examination of the portion of lung removed showed collapse, fibrosis, and bronchiectatic changes. The operation was complicated by clot formation in the pleural space and then by infection with *Staphylococcus aureus*. After open drainage, an apical thoracoplasty was done to close the residual space. The patient remained well and at work for three years and then again complained of pain in the right side of the chest. Shortly afterwards he developed a discharging sinus near the anterior end of the thoracotomy wound. Pus from the sinus contained typical 'sulphur granules' and on culture gave a growth of *A. Israeli*. There was no evidence on the chest film of disease of the ribs, and sinograms failed to demonstrate any deep extension of the sinus.

The patient was hypersensitive to penicillin and was treated with tetracycline, 2.0 g daily for six weeks. The sinus dried up and the patient refused further treatment. Three years later the sinus recurred. On this occasion no 'sulphur granules' were seen in the pus and cultures were negative for Actinomycetes. The sinus quickly dried up and again the patient refused treatment. However, the sinus has discharged

pus for a few days on two occasions since then. On neither occasion were Actinomycetes grown from the discharge. The patient attends the follow-up clinic only irregularly and always refuses to consider long term treatment.

**Comment** This is the only case in the series with the classical features of pain and a chronic discharging sinus. The intermittent re-opening of the sinus suggests that the actinomycotic infection may be latent, but it proves impossible to get this patient to take further treatment.

During the period when these six cases of infection with *A. Israeli* were encountered, we have seen one case of infection with aerobic Actinomycetes.

**CASE 7** B. C., a 52-year-old man of Indian race, has been living in Kenya until six months before admission to hospital. He first complained of weight loss and of pain in the knees, ankles, and elbows. He was found to be diabetic and when the diabetes was controlled all symptoms subsided. However, one month later he developed fever, cough, and dyspnoea. The chest film then showed consolidation and cavitation in the left upper lobe of the lung (Fig. 16). Sputum cultures gave a growth of *Nocardia asteroides* but no other pathogenic organism. *In vitro* the organism was sensitive to cephaloridine (Ceporin), sulpham

methoxazole (Septrin), and fusidic acid (Fucidin) but not to any other common antibiotic. Treatment was given with cephaloridine and sulphamethoxazole and after four weeks it was no longer possible to grow *Nocardia* from the sputum. However, the clinical state of the patient did not improve; the diabetes proved difficult to control, the abscess in the left lung did not clear, and chest radiographs showed developing infiltration on the right side. The patient died five months after admission. Permission for necropsy could not be obtained.

*Comment* Infection with *Nocardia* is even less common than infection with *A. Israeli*. As with actinomycosis, so *Nocardia* infections tend to occur in association with debilitating conditions. Nocardiosis has been reported in association with long-term steroid therapy, tuberculosis, carcinoma, and chronic suppuration. In the case reported here, diabetes may have been important.

Compared with actinomycosis, *Nocardia* infections are likely to be generalized. Almost all systems of the body have been reported to be involved. Murray, Finegold, Froman, and Will (1961), in a review of 179 cases, found that the lungs alone were involved in 31% of cases, but that the lungs were also involved in a further 30% of the cases with generalized infection. *In vitro* *N. asteroides* has been found sensitive to a variety of drugs, sulphonamides (Conant, 1958), tetracycline and chloramphenicol (Murray *et al.*, 1961), and cycloserine (Bronner and Bronner, 1969). The clinical use of these drugs has not, however, always been effective and there is a mortality of approximately 50% in the reported cases.

Animal studies have suggested that sulphadiazine may be the most effective. Marcovitch and Norman (1970) and Baike, Macdonald, and Munday (1970) each report a cure using sulphamethoxazole. Black and McNellis (1970) state that *Nocardia* is not sensitive *in vitro* to trimethoprim. We had no success with sulphamethoxazole in our case.

#### ACTINOMYCOSIS ASSOCIATED WITH BRONCHIAL CARCINOMA

In the review period, sputum from patients undergoing investigation of unidentified pulmonary opacities was routinely cultured for fungi, as well as for pathogenic bacteria. In only seven additional cases were sputum cultures positive for *A. Israeli* obtained. Five of these seven were found to be suffering from a primary bronchial carcinoma, one had carcinoma of the stomach with pulmonary and pleural spread, and in one there was no abnormality on a chest film. In the patient with the normal chest film, no lesion developed over a period of six months' observation. Garrod (1952) pointed out that the finding of *A. Israeli* in sputum cultures cannot prove the existence of invasive pulmonary disease. Kay (1948) found *Actinomyces* in the sputum of 65 of 240 patients suffering from miscellaneous bronchopulmonary infections. Slack (1942) found cultures

positive for *Actinomyces* in 14% of tonsils removed at routine operations. In our series, all except one of the patients in whom there was a chance finding of *Actinomyces* on sputum culture were suffering from co-incident pulmonary malignant disease. Undoubtedly *Actinomyces* tend to colonize devitalized tissue and so might be expected to occur within breaking down neoplasms. Three of the five bronchial carcinomata in which *Actinomyces* were found in the sputum were breaking down carcinomata. Actinomycotic infection may complicate the treatment of bronchial carcinoma, as is shown by the report of case 8.

CASE 8 W. T., a 54-year-old herdsman, had a history of dyspnoea and cough with occasional haemoptyses of two months' duration. A chest radiograph showed collapse of the right middle and lower lobes of the lung. Bronchoscopy identified a squamous-cell carcinoma in the intermediate bronchus. A right pneumonectomy was performed. The patient developed a bronchopleural fistula six days after operation. The bronchial stump was resutured and a right thoracoplasty was done. The bronchopleural fistula recurred five days after the second operation.

Two days before the re-opening of the fistula, sputum cultures gave a growth of *A. Israeli*. From then onwards *A. Israeli* was found repeatedly in sputum and cultures of the discharge from the drainage tube. The patient was treated with intramuscular penicillin, 6 million units daily for four weeks, followed by tetracycline, 1.0 g daily for 12 weeks. The bronchopleural fistula closed and the discharging sinus dried up. The patient died from generalized recurrence of the bronchial carcinoma one year after operation. We assume that the actinomycotic infection played a part in the production of the bronchopleural fistula.

#### DISCUSSION

Formerly, the common presentation of thoracic actinomycosis, as elsewhere in the body, was as a chronic discharging sinus. Recently, there has been a general reduction in the incidence of pulmonary sepsis. Co-incidentally pleuropulmonary actinomycosis with sinuses discharging pus containing 'sulphur granules' has become rare. We encountered one such case. It is still likely that the mouth is the site of primary infection. McQuarrie and Hall (1968) found dental sepsis in each of their nine cases of thoracic actinomycosis. All but three of our cases were edentulous. We were unable to recover *Actinomyces* from gum or throat swabs in any of the cases. Bramley and Orton (1960) did not find oral sepsis a feature of their cases, even of the cervicofacial type. Nevertheless, improved oral hygiene has probably played a large part in the general reduction of pulmonary sepsis as well as reducing the incidence

of actinomycosis associated with sepsis. Probably the most common presentation of thoracic actinomycosis is as a shadow on a chest radiograph similar to that caused by a bronchial carcinoma. Many reports of cases treated by resection, on the presumptive diagnosis of bronchial carcinoma, have appeared (Kugel, Harlacher, and Hueck, 1953; Pritzker and MacKay, 1963; Villegas and Sala, 1965; Moore and Scannell, 1968). Halseth and Reich (1969) report two further cases treated by lobectomy and review 28 cases of resection for actinomycosis collected from the English literature. They note that four cases developed bronchopleural fistula and empyema and that these were cases in which adequate postoperative antibiotic treatment was not given.

Resection would seem to be a reasonably safe form of treatment provided the operation specimen is examined soon after removal and the diagnosis of actinomycosis is made in time for antibiotic therapy to be given early in the post-operative period. Our cases 1 and 2 demonstrate that in the less chronic form of the disease complete resolution of the condition can be obtained with antibiotic treatment. The less chronic forms are those most likely to mimic carcinoma of the bronchus and medical treatment must be preferable to resection, if the diagnosis can be made with reasonable certainty. McQuarrie and Hall (1968) considered that the examination of sputum or bronchial washings was not helpful in determining the aetiology of suspected cases of thoracic actinomycosis. We have, however, found the cytological examination of the sputum, as practised for bronchial carcinoma, helpful in suspecting a diagnosis of actinomycosis. Our routine technique for sputum cytology is to fix the specimen in Bouins' fluid (commercial formalin 25 parts, glacial acetic acid 5 parts, saturated aqueous picric acid 70 parts) and to examine stained sections. In this way it is possible to identify 'sulphur granules' in the sputum (Figs. 2 and 3). The granule would not be so likely to remain intact when using a smear technique. If at least four representative sputum specimens are carefully examined the cytological diagnosis is about 85% accurate for bronchial carcinoma (Oswald, Hinson, Canti, and Miller, 1971). If therefore bronchoscopy and sputum cytology are negative for carcinoma but fungi are found, it would seem reasonable to give a trial of treatment. We noted diminution in the shadowing on a chest radiograph within four weeks. It must be remembered that actinomycosis can co-exist with bronchial carcinoma, but in our cases with this association there was no difficulty in establishing the diagno-

sis of bronchial carcinoma by bronchial biopsy or sputum cytology.

For many years penicillin by intramuscular injection has been the standard treatment for thoracic actinomycosis. There is, however, no agreement about the dosage required. Halseth and Reich (1969) used 20 million units a day for six weeks. McQuarrie and Hall (1968) gave courses varying from one to 20 million units daily for periods varying from 28 to 90 days. Prather, Eastridge, Hughes, and McCaughan (1970) also gave courses of between 2 and 20 million units daily for periods of 21 to 45 days.

Bates and Cruickshank (1957) recommended six million units of crystalline penicillin daily for six weeks followed by 600,000 units of penicillin for six weeks. In our case 5 prolonged low-dosage penicillin proved inadequate, admittedly following a rather short initial high-dose course. Long courses of high-dosage intramuscular penicillin are very distressing for the patient. Several other forms of treatment have been tried. McVay and Sprunt (1953) and Lesney and Traeger (1959) have reported successful treatment of cervicofacial cases with isoniazid. Bramley and Orton (1960) and O'Mahoney (1966) used tetracycline in courses of 1.0 g daily for three to five weeks with good results. It is generally agreed that cases of cervicofacial infection do not require as prolonged a course of treatment as the thoracic form. Coodley (1969) reported a patient with thoracic actinomycosis who showed no response after receiving tetracycline for three weeks, but the infection cleared on penicillin therapy.

McQuarrie and Hall (1968) treated one pulmonary case successfully with tetracycline, 2.0 g daily for a period of 73 days, and in our case 1 resolution occurred with tetracycline alone. More recently, Mohr, Rhoades, and Muchmore (1970) have successfully treated four cases (two of which were pulmonary infections) with lincomycin, 2.0 g daily for periods of 6 to 12 months.

Probably the response to therapy is determined by the chronicity of the infection. Actinomycosis can be seen to cause very dense fibrosis in the chest, so that it must be difficult to obtain high concentrations of the antibiotics at the site of infection. Our case 3 received numerous courses of tetracycline, also two courses of INAH, yet viable fungi were present at the time of operation. Also case 5, in whom infection would seem to have been present for a considerable time, responded only after a course of intravenous penicillin. Oral antibiotics are a reasonable form of treatment for pulmonary infiltration not of long standing, but treatment should be given in high dosage

for about six months. For very chronic cases prolonged high-dosage penicillin may still be the best form of treatment.

We should like to thank Dr. C. M. Connolly for the details of case 7; Dr. N. S. Mair for bacteriological reports; Mr. J. Grenfell for the photographic reproductions; and Mrs. R. C. Pitts for secretarial assistance.

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