Eur Respir J 2003; 21: 545–551
DOI: 10.1183/09031936.03.00089103

European Respiratory Journal
ISSN 0903-1936

SERIES "UNUSUAL PULMONARY INFECTIONS"
Edited by M.A. Woodhead and A. Ortqvist
Number 2 in this Series

Pulmonary actinomycosis

G.F. Mabeza, J. Macfarlane

Pulmonary actinomycosis. G.F. Mabeza, J. Macfarlane. ©ERS Journals Ltd 2003.
ABSTRACT: Pulmonary actinomycosis is a rare but important and challenging diagnosis to make. Even when the clinical suspicion is high, the disease is commonly confused with other chronic suppurative lung diseases and with malignancy.

An early, accurate diagnosis will prevent the considerable psychological and physical morbidity, including unwarranted surgery, associated with delayed diagnosis.

The clinical, radiological and therapeutic characteristics of the infection are reviewed here.

Respiratory physicians should be aware of this important differential when investigating patients for persistent pulmonary shadowing. This will expedite the diagnosis of an otherwise highly treatable condition with an excellent prognosis if picked up early.
Eur Respir J 2003; 21: 545–551.

Nottingham City Hospital, Nottingham, UK.

Correspondence: J. Macfarlane, Nottingham City Hospital, Hucknall Road, Nottingham, UK NG5 1PB.
Fax: 44 1159627723
E-mail: john.macfarlane@tinyworld.co.uk

Keywords: Actinomycosis, pulmonary, sulphur granules

Received: September 29 2002
Accepted after revision: October 25 2002

Actinomyces spp. are higher prokaryotic bacteria belonging to the family Actinomyceataceae. When they were first described in the early 19th Century, they were misclassified as fungi [1]. The name A. bovis was given to a ray-like organism found in purulent material obtained from cattle mandibles; the word "actinomycosis" was derived from the Greek terms *aktino*, which refers to the radiating appearance of a sulphur granule, and mykos, which labels the condition a mycotic disease. The first published clinical description of the human form of the disease appeared in 1857 [2]. The thoracic form was described 25 yrs later, but it was not until 1891 that *A. israelii*, the main species responsible for the human disease, was isolated [3]. The classic clinical picture of the disease actinomycosis is that of its commonest form, the cervicofacial type, in which a middle-aged male patient presents with a large mass on the jaw, not too dissimilar to the lumpy disease originally described in cattle. In fact, the infection can involve virtually every organ or body site (table 1).

Pulmonary actinomycosis is a difficult condition to diagnose. Even among experienced physicians, sometimes despite pointers to the disease, delayed diagnosis or misdiagnosis as tuberculosis, lung abscess or lung cancer is common [12]. The epidemiological, clinical, diagnostic and therapeutic characteristics of the disease are reviewed here. An increased awareness of the infection may expedite diagnosis and prevent undesirable complications, including unwarranted surgery, in patients under investigation for persistent pulmonary shadowing.

Epidemiology

Actinomycosis has been reported around the world. Although there is little accurate prevalence data in the literature, the incidence of all forms of actinomycosis appears to have declined markedly in the last three to four decades [12]. The pulmonary form of actinomycosis constitutes ~15% of the total burden of disease, although estimates of up to 50% have been reported [12–15]. It is now a rare infection, particularly in the developed world. In the current authors' 1,100-bed teaching hospital (Nottingham City Hospital, Nottingham, UK), serving a large metropolitan area in the UK and acting as a regional centre for thoracic surgery, pulmonary actinomycosis was diagnosed histologically in only four cases over a 15-yr period (I. Soomro, Dept of Histopathology, City Hospital, Nottingham, UK, personal communication). Table 2 summarises all series of pulmonary actinomycosis

Table 1. – The main forms of human actinomycosis

Type of actinomycosis	Prevalence %	[Ref.]
Cervicofacial	50–60	[4]
Pulmonary	15	
Abdomino-pelvic	20	[5]
CNS[#]	2	[6]
Cutaneous	Rare	[7]
Ophthalmic[¶]	Very rare	[8]
Cardiac[+]	Very rare	[9]
Genitourinary[§]	Very rare	[2]
Disseminated[ƒ]	Very rare	[10, 11]

CNS: central nervous system. [#]: includes cerebral abscesses, basilar meningitis and meningo-encephalitis; [¶]: includes lacrimal canaliculitis; [+]: includes pericarditis, myocarditis and endocarditis; [§]: includes pelvic inflammatory disease and epididymorchitis; [ƒ]: multiple organ involvement including osteomyelitis and septic arthritis.

Previous articles in this series: No. 1: Tärnvik A, Berglund L. Tularaemia. *Eur Respir J* 2003; 21: 361–373.

Table 2. – Summary of cases of pulmonary actinomycosis in the adult English literature[#] (January 1980–January 2002)

First author [ref.]	Year	Cases n	Strong suspicion of malignancy n	Diagnosis				Treatment	
				FNA	Brochial biopsy[¶]	Surgery	Other	Medical[+]	Medical[§]
NEWSOM [16]	1982	7	No data	0	0	5	2	0	7
JENSEN [17]	1989	9	3	0	0	6	3	0	9
KINNEAR [18]	1990	19	9	2	0	7	10	12	7
KWONG [19]	1992	8	No data	1	0	7	0		No data
HSIEH [20]	1993	17	8	3	4	9	1	8	9
TASTEPE [21]	1998	7	4	0	0	7	0	0	7
DUJNEUNGKUNAKORN [22]	1999	16	4	1	10	5	0	6	10
RIZZI [23]	1996	13	6	0	0	12	1	1	12
CHEON [24]	1998	22	2	9	4	9	0		No data
YEW [25]	1999	8	No data	1	7	0	0	8	0
BAIK [26]	1999	25	11	8	1	13	1	11	14

FNA: percutaneous fine-needle aspiration or core biopsy. [#]: Medline search used with pulmonary, thoracic as search criteria to find series with five or more patients; [¶]: including transbronchial biopsy; [+]: medical (antibiotic) treatment only; [§]: surgery followed by medical treatment (none of the patients had surgical treatment only).

with more than five cases reported in the adult English language literature in the last two decades.

The presentation of pulmonary actinomycosis has also changed. It now appears less aggressive in nature compared with the pre-antibiotic era [12]. These changes in both the disease′s presentation and its incidence may be the result of improvements in oral hygiene, in the ready availability of antibiotics and in the early initiation of treatment when pulmonary infection is suspected. *Actinomyces* spp. are sensitive to several antibiotics in common use [27]. In the developing world, where healthcare resources are limited, it is possible that the incidence of the disease may be higher, but accurate data are lacking. Even in the developed world, the disease′s incidence may be an underestimation; the diagnosis is quite difficult to make in the first place and it is possible some early cases are being inadvertently treated and cured when antibiotics are given for other reasons [28]. Somewhat surprisingly, socioeconomical class *per se* does not appear to correlate with disease incidence in the developed world [29].

Pulmonary actinomycosis occurs at all ages, although it is very unusual in children. A bimodal age distribution with an earlier peak at ages 11–20 has been described, but most series describe a clear peak incidence in the 4th and 5th decades [2, 30]. BATES and CRUICKSHANK [31] reported finding only 27% of all forms of actinomycosis infections occurring in individuals >20 yrs of age. The incidence of infection is two to four times greater in males compared with females [2]. This disparity has been partly attributed to poorer oral hygiene and/or a higher incidence of facial trauma in males resulting in dental and facial disease. These may also be risk factors for the thoracic form [28]. A higher incidence of pulmonary actinomycosis has also been reported in patients with underlying respiratory disorders, such as emphysema, chronic bronchitis and bronchiectasis, and in alcoholics, but the series were small [8, 30]. Despite references to the contrary, *Actinomyces* spp. have been demonstrated in nature outside of an animal or human host [32]. However, no person-to-person transmission or racial, seasonal or occupational predilection has been demonstrated [12, 33].

Pathogenesis

Microbiology: organisms involved

Members of the genus Actinomyces are Gram-positive, nonspore-forming, predominantly anaerobic prokaryotic bacteria belonging to the family Actinomyceataceae. They are bacteria rather than fungi for a variety of reasons: they replicate through bacterial fission rather than by budding, they lack sterols in their cell walls, they are resistant to polyene antifungal agents and they are sensitive to standard antibacterial agents such as penicillin [2]. Actinomyces spp. are commensals of the human oropharnynx, gastrointestinal tract and female genitalia, and are often routinely cultured from these mucosa-lined orifices. Fourteen species have been clearly characterised to date [28]. Six of these are thought to be pathogenic in humans, including A. israelii, A. naeslundi, A. odontolyticus, A. viscosus, A. meyeri and A. gerencseriae. A. israelli is the organism most commonly incriminated in human disease. In contrast to other species, A. meyeri may have a greater tendency for affecting the lung and haematogenous dissemination. This propensity for dissemination is difficult to explain; A. meyeri is no different from the other species in its microbiological characteristics [34]. In addition to these traditional actinomycotic forms, some coryneform anaerobic bacteria have also recently been assigned to the genus Actinomyces by the Centres for Disease Control (CDC) in the USA [35, 36]. Their pathogenic role in humans remains unclear [37]. A. bovis, the causative agent in bovine infections, is generally not considered to be a human pathogen. Arachnia propionica, from the related genus Arachnia, is also a well-established cause of actinomycosis.

Depending on the site of infection, most cases of actinomycosis yield a variety of other microorganisms on culture, in addition to *Actinomyces* spp.

Acinobacillus actinomycetesmcomitans, *Eikenella corrodens*, Enterobacteriaceace, and species of Fusobacterium, Bacteroides, Capnocytophagia, Staphylococci, and Streptococci have all been isolated with *Actinomyces* spp. in various combinations [38]. An average of two to four and sometimes up to 10 of these concomitant species are usually found in association with the causative actinomycete. Their contribution to the pathogenesis in actinomycosis is unclear. While they are generally regarded as nonpathogenic in the context of actinomycosis, the possibility remains that the disease actinomycosis may be caused by a polymicrobial infection in which *Actinomyces* spp. predominate [8, 39]. It is possible that these other organisms enhance the pathogenicity of actinomycetes by creating an anaerobic millenuea in which Actinomyces thrives. This may be due to the reduction of oxygen tension in tissues and through anaerobiosis-induced inhibition of phagocytes [12]. Implications of this for treatment will be discussed later.

Culture and staining characteristics

Actinomyces are fastidious bacteria that are difficult to culture. Bacterial confirmation of a clinico-pathological diagnosis is usually obtained in <50% of cases due to inadequate culturing technique, previous antibiotic therapy and bacterial overgrowth, even when the clinical suspicion is high [2]. Actinomyces are sensitive to most of the antibiotics used in everyday practice; even a single dose of an antibiotic before culture may inhibit the organism′s growth [27]. Correct techniques for collecting and delivering tissue specimens for anaerobic culture are vital, as is communication between the clinician and the microbiologist. Culture requires brain/heart-enriched agar and the organisms grow best at a temperature of 37°C in an atmosphere of 6–10% ambient carbon dioxide. *A. viscosus* is unique because it grows under microaerophilic or aerobic conditions. A few strains of *A. israelii* are also microaeropholic. Characteristically, colonies of Actinomyces appear as "molar-tooth" or "bread-crumb" colonies in broth media after 3–7 days of incubation. For adequate growth, however, cultures should be observed for up to 21 days. Differentiation of the species is difficult, requiring assessment of several metabolic capabilities. Fluoroscein-conjugated antibody typing is now available for species differentiation in some centres [28].

Actinomyces stain in tissue with Gomori methenamine silver and the Brown and Brenn modification of the Gram stain [8]. Most of the literature classifies the tissue response as granulomatous or "granulomatoid-like", although giant cells and granulomata are rarely seen [39]. Sulphur granules are the pathological hallmark of the disease. These are round or oval basophilic masses with a radiating arrangement of eosinophilic clubs on the surface; they sometimes can be seen even with a magnifying glass. The name "sulphur granule" has its origin in the small nodules resembling elemental sulphur that were commonly used in pharmaceuticals in the 19th century [4]. Although they are usually highly suggestive of actinomycosis, they are not diagnostic on their own; they are also seen in nocardiosis, chromomycosis, eumycetoma and botryomycosis, albeit very rarely [39].

Pathogenesis

A vital step in the development of actinomycosis is the disruption of the mucosal barrier, allowing the organisms to invade. For cervicofacial and abdominal actinomycosis, such a break may result from dental sepsis, appendicitis, diverticulitis, trauma or surgery [4]. For pelvic disease it may result from the use of intra-uterine or intravaginal devices [5]. Pulmonary actinomycosis probably results from aspiration of oropharyngeal or gastrointestinal secretions into the respiratory tract [2]. Poor oral hygiene and associated dental disease may increase the risk [12]. Support for aspiration as a risk factor comes from reports of a higher prevalence of alcoholism in patients with the pulmonary form of the disease and from the basilar predominance of the disease radiologically [10]. In the pre-antibiotic era, transdiaphragmatic spread of infection from the abdomen was an important route in thoracic actinomycosis, but this is probably no longer so [2, 12]. Infection as a result of distant haematogenous seeding, lymphatic spread or spread from the neck through the mediastinum is also now very rare [10]. The haematogenous route of dissemination may be a more important source in paediatric thoracic actinomycosis, where the disease has been noted to occur in apparently healthy children with "good" dental health [14, 15].

Pulmonary actinomycosis probably starts when saliva, or other material laden with *Actinomyces* spp., is aspirated into a minor bronchus, causing atelectasis and a pneumonitis. Once established, the initial acute inflammation is followed by the characteristic chronic, indolent phase that generates local necrosis and fibrosis and commonly cavitates [39]. It progresses slowly with little regard for anatomic boundaries, crossing interlobar fissures. It is not clear how much of this propensity to spread is related to the bacteria′s proteolytic enzymes, some reports having shown a relative paucity of these [30]. If unchecked, the disease invades the pleura, chest wall, soft tissues and bony structures; sinus tracts may form, opening and closing spontaneously.

Diagnosis

It is important to make a diagnosis of pulmonary actinomycosis. Although it is now a rare disease with a very low mortality rate [12], early accurate diagnosis will prevent the considerable morbidity, both psychological and physical, associated with either delayed or missed diagnosis. Misdiagnosis, particularly for a malignancy, is distressing for the patient who may end up with a thoracotomy and lung resection for essentially a benign and curable disease. Yet the diagnosis can be quite a challenge. In one series, the diagnosis was suspected on admission in <7% of patients who later turned out to have the infection [29]. The average duration of illness before definitive diagnosis was ~6 months, a consistent figure in most series [29]. Even when the clinical suspicion is high, microbiological confirmation can still be difficult, as has been already alluded to. The disease shares many similar clinical features with chronic suppurative lung infections, such as tuberculosis, fungal infections and lung abscesses, and also lung malignancy with which it is commonly confused. Up to a quarter of cases of thoracic actinomycosis are initially diagnosed as malignancy. To confound matters, the disease can coexist with lung-cancer, as *Actinomyces* spp. have a tendency to colonise devitalised tissue, which commonly occurs within necrotic neoplasms [40]. Finding Actinomycetes filaments in sputum alone, particularly without the characteristic sulphur granules, may therefore represent simple colonisation. Thus, short of exploratory thoracotomy, differentiation from lung carcinoma may sometimes be impossible. The diagnosis therefore requires a combination of several factors, including a positive culture and demonstration of sulphur granules in purulent matter from infected tissue, correlation with the clinical and radiological features, and the response to antibiotic treatment.

Clinical features

In 1957, BATES and CRUICKSHANK [31] described a fairly dramatic presentation of pulmonary actinomycosis with prominent chest pain and cutaneous fistulas discharging sulphur granules. This mode of presentation has changed with time in line with the decrease in the disease′s prevalence [40, 41]. The commonest presentation is probably now as a shadow on a chest radiograph, similar to that caused by bronchial carcinoma. In a previous review of thoracic actinomycosis in five health regions in the UK, the current authors found the three commonest complaints to be cough, sputum and chest pain (table 3). While chest pain was a prominent symptom and may act as a pointer to actinomycosis, the disease′s symptoms are still quite nonspecific and similar to those of other chronic suppurative chest diseases and malignancy. In a patient known to have pulmonary actinomycocis, marked weight loss, malaise and high fever may be more suggestive of disseminated disease [10, 11]. Physical signs are equally nonspecific, except in advanced, untreated disease, when sinuses

Table 3. – Typical symptoms of patients with thoracic actinomycosis

Symptoms	Patient % (n)
Respiratory	
Cough	84 (16)
Sputum	74 (14)
Chest pain	68 (13)
Dyspnoea	47 (9)
Haemoptysis	31 (6)
Localised chest-wall swelling	10 (2)
Systemic	
Weight loss	53 (10)
Malaise	42 (8)
Night sweats	32 (6)
Fever	21 (4)

Adapted from data on 19 patients described in [28].

and fistulae may then give the diagnosis away. The findings are occasionally those of the associated complications, such as pleural effusion or empyema.

Immunosuppression and pulmonary actinomycosis

Considering the impairments in both cellular and humoral immunity that accompany the human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) infection, it is somewhat surprising that the reported incidence of actinomycosis in this group of patients has remained low [42]. This fact was recognised early in the course of the epidemic and has subsequently been borne out in more recent studies. While a plethora of other rare granulomatous opportunistic infections have been associated with the AIDS pandemic, there were only 17 reported cases of all forms of actinomycosis in the English literature between 1996 and December 1999 [42]. Only three of these were pulmonary and even then there was no clear correlation with degree of immunosuppression [43–45]. The reason for this is not clear. It is possible the disease is under-diagnosed in this group of patients. Actinomycosis is an infection that is difficult to diagnose even in immunocompetent patients; it may be even more difficult to diagnose in the setting of HIV/AIDS where there are a myriad of other infections with similar indolent and nonspecific presentations. It may also be a reflection of the widespread use of antibiotics in this population, leading to resolution of undiagnosed actinomycotic infection. Younger people also tend to have better dental hygiene and so it is possible that this risk factor is smaller in the predominantly younger group affected by HIV/AIDS, but there is no objective evidence for this. When the disease does occur in HIV/AIDS, its clinical presentation appears similar in pattern to that in immunocompetent people and it appears to respond to the conventional treatment regimens [42]. Pulmonary actinomycosis has also not been convincingly shown to have an increased prevalence among other immunocompromised hosts, such as those on chronic steroid therapy, cancer chemotherapy or immunosuppressive therapy postorgan transplant [2, 12]. As already alluded to, anecdotal reports have suggested an increased prevalence of the disease in patients with underlying lung disease and alcoholism [8, 30].

Laboratory tests

Basic tests reflect the nonspecific inflammatory nature of the illness. There is usually a mild leukocytosis, predominantly polymorphonuclear, and, depending on the duration of the illness, a normochromic anaemia. The erythrocyte sedimentation rate and the C-reactive protein may be moderately raised as with any chronic disease and these probably do not confer any diagnostic advantage.

Radiology

Radiological pulmonary actinomycosis can resemble a spectrum of lung pathologies ranging from benign infection to metastatic tumour. The main problem is distinguishing the disease from a neoplasm [46]. Although, in experienced hands, some forms of imaging may show features more suggestive of actinomycosis, or at least an inflammatory process, than a neoplasm [47], imaging modalities on their own are not diagnostic. Definitive diagnosis is still based on histological or microbiological conformation. Imaging is useful in evaluating the exact location and extent of disease to help direct accurate biopsy and to monitor response to treatment. Irrespective of the imaging modality, a few general principles apply. First, the radiological findings depend on the duration of the infection; in the early stages of the infection, the findings are usually indistinguishable from those of any other pneumonic process. Secondly, the disease usually shows a peripheral and lower lobe predominance, probably reflecting the role of aspiration in its pathogenesis [19]. Finally, the disease usually shows some diminution in size within 4 weeks of starting treatment [40].

Plain radiograph

Plain chest radiograph findings in actinomycosis are nonspecific. A nonsegmental pneumonia, usually in the lower zones, tends to occur peripherally crossing fissures. However, the spectrum of changes is wide, ranging from a few pulmonary infiltrates to cavitating mass lesions involving the pleura, chest wall or even vertebral spine [48, 49].

Computerised tomography and magnetic resonance imaging

There is limited information on both computed tomography (CT) and magnetic resonance imaging (MRI) findings in pulmonary actinomycosis [48, 50]. Most of the published series are small retrospective studies. The CT is probably more helpful than the plain radiograph, particularly if performed with a bone window display, which gives a better delineation of minimal bony change, such as early rib erosion and osteomyelitis. These may be easily missed by plain chest radiography. A range of findings have been described on CT in pulmonary actinomycosis, including patchy air-space consolidation, multifocal nodular appearances, cavitation, pleural thickening, pleural effusions and hilar, and/or mediastinal lymphadenopathy [48, 49, 51]. Mediastinal lymphadenopathy may be more common than previously thought [19]. Consolidation with involvement of adjacent pleura and chest wall, and pulmonary infiltrates with air bronchograms or so-called "air sign", may be more suggestive of thoracic actinomycosis [30, 47, 49]. Associated pleural effusions tend to be small to moderate in size rather than massive [15]. Very occasionally, pericardial effusion results from pericardial involvement or pericarditis [52, 53].

Although there is considerable data on the use of MRI in other forms of actinomycosis, such as in the central nervous system, there is little data for its use in the thoracic form [50]. Part of the reason may be the attendant problems associated with imaging the chest using MRI.

Isotope scanning

Anecdotal reports have shown unexpected focal uptake of certain isotopes in pulmonary actinomycotic lesions [54, 55]. There is insufficient data to make sensible comments about the usefulness of such investigations in routine clinical practice.

Bronchoscopy

Fibreoptic bronchoscopy is usually not diagnostic in pulmonary actinomycosis unless there is clear endobronchial disease on which biopsy can be performed [17]. Simple culture of the bacteria in bronchoalveolar secretions alone, as with sputum, is inadequate for the diagnosis as it may represent mere colonisation [56]. Bronchoscopy is still a useful investigation however, particularly in excluding lung malignancy. Endobronchial actinomycosis may manifest as irregular granular thickening and partial occlusion of bronchi, which resembles submucosal tumour, yet may only demonstrate nonspecific chronic inflammation histologically. It may also be florid disease, showing an exophytic mass with a purulent exudates and characteristic histology with sulphur granules [44]. The method of obtaining a bronchial sample is important. The sample should be procured anaerobically with a protected specimen brush [28]. Ordinary bronchoalveolar lavage culture, which is not obtained routinely under anaerobic conditions, may be falsely negative if exposed to air for more than 20 min. Transbronchial biopsies have not been successful in providing diagnostic material for thoracic actinomycosis [18, 57].

Lung biopsy

Some form of lung biopsy is usually necessary to obtain uncontaminated samples for histological and microbiological conformation of pulmonary actinomyocosis [2]. The challenge for the clinician is to obtain this in the least invasive fashion. Traditionally, excisional biopsy was the definitive diagnostic procedure [40]. In general, an attempt at establishing diagnosis by percutaneous biopsy with fine needle aspiration or core biopsy is now made before "blind" thoracotomy [58]. When guided by ultrasound or CT, this has proven a simple, safe and effective diagnostic technique and reduced the number of unnecessary resections [59–61]. Sometimes reassurance that the patient does not have a malignancy can only be provided by open resection. In these few patients, if the diagnosis is suspected pre-operatively, the aim should be to conserve as much of the lung as possible. Since the gross appearance of the pulmonary actinomycosis intraoperatively is indistinguishable from that of carcinoma, a frozen section, on a wedge resection or surgical trucut biopsy, may help in deciding the extent of the resection [59, 60]. It is still important to alert the pathologist of the suspected diagnosis, as special stains may have to be used to look for the organism [59].

Treatment

Sulphonamides were the real first breakthrough rationale drug therapy in actinomycosis in the late 1930s, until they were superseded by penicillin, which has remained the drug of choice over the last 50 yrs. Before that, a whole variety of unproven remedies had been tried, including potassium iodide (KI), radiation treatment and thymol and copper. KI was used because of an early misconception that the Actinobacillus in cattle, which is sensitive to KI, was the causative agent in humans. Actinomyces is insensitive to KI [62]. Thymol and copper were popularised for their astringent properties before the availability and acceptance of antibiotics. When the disease is diagnosed early, pulmonary actinomycosis is a relatively easy disease to treat with an excellent prognosis. The duration of treatment is less clear.

The rationale for the use of penicillin in actinomycosis is based more on extensive successful clinical experience over the last 50 yrs than on randomised control trials [12]. The main principle of treatment is the use of high-dose intravenous penicillin for a long duration of treatment. Although treatment has to be tailored to the individual, generally 18–24 million units of penicillin per day are given for 2–6 weeks followed by oral therapy with penicillin V (or amoxicillin) for 6–12 months. In general, the thoracic form appears to require longer treatment courses compared to the other commoner forms [40]. Tetracyclines are the alternative especially for penicillin-allergic patients. In pregnant, penicillin-sensitive patients, erythromycin is a safe alternative. Other alternatives, which are probably effective, but for which there is less extensive clinical experience, are shown in table 4.

Presumably, the avascularity and induration of infected areas account for the need for prolonged treatment and undoubtedly longer courses minimise the risk of relapses, a clinical hallmark of the infection. Response to treatment should be monitored radiologically with plain radiographs and/or CT. Diminution in the shadowing on a chest radiograph is expected within 4 weeks. Coexistent bronchial carcinoma should be suspected in case of medical treatment failure [22]. Evidence shows that this standard treatment approach applies to people who are immunocompromised for one reason or another [42]. Several newer antimicrobial agents have been tried with an emphasis on shorter courses of treatment (table 4). Although there are anecdotal reports of success with this approach, there is limited clinical experience and only randomised trials, which are probably impractical, would resolve this question.

The question of whether to treat the co-pathogens usually associated with Actinomycetes is not completely resolved. Some have advocated designing initial antibiotic regimens to specifically target these organisms as well. Interestingly, although most of these organisms are not sensitive to penicillin *in vitro*, they are usually eradicated (clinical cure) when the antibiotic is administered [29]. It is probably not necessary to use additional antibiotics.

Table 4. – Commonly used antibiotics and efficacy in the treatment of actinomycosis

Antibiotic	MIC range mg·mL^{-1}	[Ref.]
Efficacious[#]		
Penicillin	⩽0.25–0.5	[63]
Tetracycline (doxycycline)	0.5–0.8	[63]
Erythromycin	⩽0.25–1	[26]
Clindamycin	⩽0.25–0.5	[26]
Probable efficacy[¶]		
Imipenem	0.125	[64, 65]
Ceftriaxone	<0.06–2	[66, 67]
Ineffective[+]		
Flouroquinolones (ciprofloxacin)	0.5–128	[63]
Metronidazole	2–>128	[63]
Aminoglycosides (amikacin)	⩽0.25–1	[26]

[#]: considerable successful clinical experience; [¶]: anecdotal successful reports; [+]: ineffective *in vitro*.

Surgery

Even with extensive pulmonary disease, medical cure should still be attempted. Nevertheless, surgery remains an important therapeutic adjunct. It is particularly useful if there are complications, such as well-defined abscesses and empyemas, or where discharging fistulas and sinuses may need to be opened up [68], or, in very rare instances, to control life threatening haemoptysis that can occur with the infection [69, 70]. When surgery has been the initial treatment, even if histology suggests complete resection, it still needs to be followed by prolonged antibiotic therapy, as surgery alone is usually not curative [71, 72]. Inadequate antibiotic therapy postoperatively may result in complications such as bronchopleural fistulas and empyema.

Prognosis

The prognosis of the pulmonary form of actinomycosis may be less favourable compared with the other commoner forms, such as cervicofacial and abdominal disease [10]. This may be related to the greater incidence of disseminated disease in the thoracic form and may also be a reflection of late diagnosis in this condition. However, when the infection is recognised early and proper treatment is given the condition has an excellent prognosis with a very low mortality [29]. Every respiratory physician should be familiar with this important differential in any patient with long-standing pulmonary infiltrates to prevent unnecessary morbidity or even unwarranted surgery.

References

1. Rippon JW. Medical Mycology. *In*: Wonsiewicz MJ, ed. The Pathogenic Fungi and the Pathogenic Actinomycetes. 3rd edn. Philadelphia, W.B. Saunders Co., 1988; pp. 30–52.
2. Bennhoff DF. Actinomycosis: diagnostic and therapeutic considerations and a review of 32 cases. *Laryngoscope* 1984; 94: 1198–1217.
3. Lerner PI. Actinomyces and arachnia. *In*: Wonsiewicz MJ, ed. Infectious Diseases. Philadelphia, W.B. Saunders Co., 1992; pp. 1626–1632.
4. Miller M, Haddad AJ. Cervicofacial actinomycosis. *Oral Surg Oral Med Oral Path Oral Radiol Endod* 1998; 85: 496–508.
5. Lippes J. Pelvic actinomycosis: a review and preliminary look at prevalence. *Am J Obstet Gynaecol* 1999; 180: 265–269.
6. Smego RA Jr. Actinomycocis of the central nervous system. *Rev Infect Dis* 1987; 9: 855–865.
7. Rivitti EA, Aoki V. Deep fungal infections in tropical countries. *Clin Dermatol* 1999; 17: 171–190.
8. Schaal KP, Lee H. Actinomycete infections in humans - a review. *Gene* 1992; 115: 201–211.
9. O'Sullivan RA, Rivers JT, Armstrong JG, Mitchell CA. Pulmonary actinomycosis complicated by effusive constrictive pericarditis. *Aust NZ J Med* 1991; 21: 879–880.
10. Apothloz C, Regamey C. Disseminated infection due to *Actinomyces myeri* - case report and review. *Clin Infect Dis* 1995; 22: 621–625.
11. de la Monte SM, Gupta PK, White CL. Systemic Actinomyces infection: a potential complication of intrauterine contraceptive devices. *JAMA* 1982; 15: 1579–1580.
12. Russo TA. Agents of actinomycosis. *In*: Mandell GL, ed. Principles and Practice of Infectious Disease. 5th edn. New York, Churchill Livingstone, 1995; pp. 2645–2654.
13. Holm P. Studies on the aetiology of human actinomycosis. II. The "other" microbes of actinomycosis and their importance. *Acta Pathol Microbiol Scand* 1951; 28: 391.
14. Hachitanda Y, Nakagawara A, Ikeda K. An unusual wall tumour due to actinomycosis in a child. *Paediatr Radiol* 1989; 20: 96.
15. Rose HD, Varkey B, Kutty CP. Thoracic actinomycosis caused by *Actinomyces myeri*. *Am Rev Respir Dis* 1982; 125: 251–254.
16. Newsom BD, Hardy JD. Pulmonary fungal infections: survey of 159 cases with surgical emplications. *J Thorac Cardiovassc Surg* 1982; 83: 218–226.
17. Jensen BM, Kruse-Anderson S, Anderson K. Thoracic actinomycosis. *Scand J Thorac Cardiovasc Surg* 1989; 23: 181–184.
18. Kinnear WJM, MacFarlane JT. A survey of thoracic actinomycosis. *Respir Med* 1990; 84: 57–59.
19. Kwong JS, Müller NL, Godwin JD, Aberle D, Grymaloski MR. Thoracic actinomycosis: CT findings in eight patients. *Radiology* 1992; 183: 189–192.
20. Hsieh M-J, Lui H-P, Chang J-P, Chang C-H. Thoracic actinomycosis. *Chest* 1993; 104: 366–370.
21. Tastepe AI, Ulasan NG, Liman ST, Demircan S, Uzar A. Thoracic actinomycosis. *Eur J Cardiothoracic Surg* 1998; 14: 578–583.
22. Dujneungkunakorn T, Riantawan P, Tungsagunwattana S. Pulmonary actinomycosis: a study of 16 cases from Central Chest Hospital. *J Med Assoc Thai* 1999; 82: 531–535.
23. Rizzi A, Rocco G, Pona CD, *et al.* Pulmonary actinomycosis: surgical considerations. *Monaldi Arch Chest Dis* 1996; 51: 369–372.
24. Cheon JE, Im JG, Lee JS, Choi GM, Yeon KM. Thoracic actinomycosis: CT findings. *Radiology* 1998; 209: 229–233.
25. Yew WW, Wong PC, Lee J, Fung SL, Wong CF, Chan CY. Report of eight cases of pulmonary actinomycosis and their treatment with imipenem-cilastatin. *Monaldi Arch Chest Dis* 1999; 54: 126–129.
26. Baik JJ, Lee GL, Yoo CG, Han SK, Shim YS, Kim YW. Pulmonary acticnomycosis in Korea. *Respirology* 1999; 4: 31–35.
27. Tanaka-Bandoh K, Watanabe K, Kato N, Ueno K. Susceptibilities of *Actinomyces* species and *Propionibacterium propionicus* to antimicrobial agents. *Clin Infect Dis* 1997; 25: Suppl. 2, S262–S263.
28. Smego RA, Foglia G. Actinomycosis. *Clin Infect Dis* 1998; 26: 1255–1263.
29. Weese WC, Smith IM. A study of 57 cases of actinomycosis over a 36-year period. *Arch Intern Med* 1975; 135: 1562–1568.
30. Heffner JE. Pleuropulmonary manifestations of actinomycosis and noardiosis. *Semin Respir Infect* 1988; 3: 352–361.
31. Bates M, Cruickshank G. Thoracic actinomycosis. *Thorax* 1957; 12: 99–124.
32. Duarte GF, Rosado AS, Seldin L, de Araujo W, van Elsas JD. Analysis of bacterial community structure in sulphurous-oil-containing soils and detection of species carrying dibenzothiophene desulfurization (dsz) genes. *Appl Environ Microbiol* 2001; 67: 1052–1062.
33. Peabody JW, Seabury JH. Actinomycosis and nocardiosis. *J Chronic Dis* 1957; 5: 374–403.
34. Hennrikus EF, Pederson L. Disseminated actinomycosis. *West J Med* 1987; 147: 201–204.
35. Finegold SM, Jousimies-Somer H. Recently described clinically important bacteria: medical aspects. *Clin Infect Dis* 1997; 25: Suppl. 2, S88–S93.
36. Funke G, von Graevenitz A. Infections due to *Actinomyces neuii* former "CDC coryneform group 1" bacteria. *Infection* 1995; 23: 73–75.
37. Mann C, Dertinger S, Hartmann G, Schurz R, Simma B. *Actinomyces neuii* and neonatal sepsis. *Infection* 2002; 30: 178–180.
38. Holm P. Studies on the aetiology of human actinomycosis. I.

The "other" microbes of actinomycosis and their importance. *Acta Pathol Microbiol Scand* 1950; 27: 736.
39. Brown JR. Human actinomycosis. A study of 181 subjects. *Human Pathol* 1973; 4: 319–330.
40. Slade PR, Slesser BV, Southgate J. Thoracic actinomycosis. *Thorax* 1973; 28: 73–85.
41. Frank P, Strickland B. Pulmonary actinomycosis. *Br J Radiol* 1974; 47: 373–378.
42. Chaudhry SI, Greenspan JS. Actinomycosis in HIV infection: a review of a rare complication. *Int J STD AIDS* 2000; 11: 349–355.
43. Ossorio MA, Fields CL, Bryd RP, Roy TM. Thoracic actinomycosis and human immunodeficiency virus infection. *South Med J* 1997; 90: 1136–1138.
44. Cendan I, Klapholz A, Talavera W. Pulmonary actinomycosis: a cause of endobronchial disease in a patient with AIDS. *Chest* 1993; 103: 1886–1887.
45. Klapholz A, Talavera W, Rorat E, Salsitz E, Widrow C. Pulmonary actinomycosis in a patient with HIV infection. *Mt Sinai J Med* 1989; 56: 300–303.
46. Allen HA III, Scatarige JC, Kim MH. Actinomycosis: CT findings in six patients. *AJR* 1987; 149: 1255–1258.
47. Ng KK, Cheng YF, Ko SF, Ng SH, Pai SE, Tsai CC. CT findings of paediatric thoracic actinomycosis; report of four cases. *J Formosan Med Assoc* 1992; 91: 346–360.
48. Webb WR, Sagel SS. Actinomycosis involving the chest wall: CT findings. *AJR* 1982; 139: 1007–1009.
49. Flynn MW, Felson B. The roentgen manifestations of thoracic actinomycosis. *AJR* 1970; 11: 707–716.
50. Wand A, Gilbert HM, Litvack B, Markisz JA. MRI of thoracic actinomycosis. *J Comput Assit Tomogr* 1996; 20: 770–772.
51. Parker JS, deBoisblanc BP. Case report: Actinomycosis: Multinodular pulmonary involvement. *Am J Med Sci* 1994; 307: 418–419.
52. Jafri SZH, Roberts JL, Bree RL. Computed tomography of chest wall masses. *Radiographics* 1989; 9: 51–68.
53. Datta JS, Raff MJ. Actinomycotic pleuropericarditis. *Am Rev Respir Dis* 1974; 110: 338–341.
54. Aktolun C, Demirel D, Kir M, Bayhan H, Maden HA. Technetium-99m-MIBI and thallium-201 uptake in pulmonary actinomycosis. *J Nucl Med* 1991; 32: 1429–1430.
55. Hoekstra CJ, Hoekstra OS, Teengs JP, Postmus PE, Smit EF. Thoracic actinomycosis imaging with fluorine-18 fluorodeoxyglucose positron emission tomography. *Clin Nucl Med* 1999; 24: 529–530.
56. Ariel I, Breuer R, Kamal NS, Ben-Dovi I, Mogle P, Rosenmann E. Endobronchial actinomycosis simulating bronchogenic carcinoma: diagnosis by biopsy. *Chest* 1991; 99: 493–495.
57. Lee C-H, Lin M-C, Tsai Y-H. Thoracic actinomycocis - review of 9 cases. *Chang Gung Med J* 1991; 14: 246–252.
58. Pauker SG, Kopelman RI. Clinical problem solving. A rewarding pursuit of certainty. *N Engl J Med* 1993; 329: 1103–1107.
59. Das DK. Actinomycosis in fine needle aspiration cytology. *Cytopathology* 1994; 5: 243–250.
60. Moore WR, Scanell JG. Pulmonary actinomycosis simulating cancer of the lung. *J Thorac Cardiovas Surg* 1968; 55: 194–195.
61. Hsu W-H, Chiang C-D, Chen C-Y. Ultrasound-guided fine needle aspiration biopsy in the diagnosis of chronic pulmonary infection. *Respiration* 1997; 64: 319–325.
62. Suter LS, Vaughan BF. The effect of antibacterial agents on the growth of *Actinomyces bovis*. *Antibiot Chemother* 1965; 5: 557–560.
63. Wade WG. *In-vitro* activity of ciprofloxacin and other agents against oral bacteria. *J Antimicrob Chemo* 1989; 24: 683–687.
64. Edelmann M, Cullmann W, Nowak KH, Kozuschek W. Treatment of abdominothoracic actinomycosis with imipenem. *Eur J Clin Microbiol* 1987; 104: 194–195.
65. Yew WW, Wong PCW, Wong CF, Chau CH. Use of imipenem in the treatment of thoracic actinomycosis. *Clin Infect Dis* 1994; 19: 983–984.
66. Skoutelis A, Petrochilos J, Bassaris H. Successful treatment of thoracic actinomycosis with ceftriaxone. *Clin Infect Dis* 1994; 19: 161–162.
67. Rolfe R, Finegold S. Comparative *in-vitro* activity of ceftriaxone against anaerobic bacteria. *Antimicrob Agents Chemother* 1982; 22: 338–341.
68. Conant EF, Wechsler RJ. Actinomycosis and nocardiosis of the lung. *J Thorac Imaging* 1992; 7: 75–84.
69. Conlan AA, Hurwitz SS, Krige A, Nicolaou N, Pool R. Massive haemoptysis: review of 123 cases. *J Thorac Cardiovasc Surg* 1983; 85: 120–124.
70. Halseth WL, Reich MP. Pulmonary actinomycosis treated by lung resection. *Dis Chest* 1969; 55: 119.
71. Harvey J, Cantrell J, Fisher A. Actinomycosis: its recognition and treatment. *Ann Intern Med* 1957; 46: 868–885.
72. Berardi R. Abdominal actinomycosis. *Surg Gynaecol Obstet* 1979; 149: 257–266.