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Actinomycosis

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Actinomycosis is a rare, chronic, and slowly progressive granulomatous disease caused by filamentous Gram positive anaerobic bacteria from the Actinomycetaceae family (genus *Actinomyces*).[1] It is often misdiagnosed because it can mimic other conditions such as malignancy and tuberculosis,[2] and a high level of clinical suspicion is needed for an early diagnosis. However, it is readily treatable and curable if the patient is appropriately managed. We review the clinical presentations of actinomycosis, its diagnosis, and approaches to treatment. Our review is based on the findings of randomised controlled trials, prospective analytical and retrospective studies, review articles, and case reports.

How is actinomycosis acquired?

Actinomyces are commensals of the human oropharynx, gastrointestinal tract, and urogenital tract. When tissue integrity is breached through a mucosal lesion they can invade local structures and organs and become pathogenic. Actinomycosis is therefore mainly an endogenous infection.[3] Actinomyces are often isolated with other normal commensals, such as *Aggregatibacter actinomycetemcomitans* (previously *Actinobacillus actinomycetemcomitans*), *Eikenella corrodens*, fusobacteria, bacteroides, capnocytophaga, staphylococci (including *S aureus*), streptococci (including β haemolytic streptococci and *S pneumoniae*), or Enterobacteriaceae, but the precise pattern of organisms depends on the site of infection.[4] Animal studies have suggested that these species help actinomyces establish an infection by inhibiting host defences, although their exact roles are not clear.[w1 w2]

How common is it and who gets it?

Anyone can be infected with actinomyces, but the disease is essentially rare—because of a lack of data, particularly in developing countries, estimates of its incidence are not recent. In the 1970s the incidence in Cleveland, USA, was reported to be one per 300 000, compared with Germany and the Netherlands in the 1960s where it was estimated to be one per million.[1] The Department of Health in the United Kingdom reported that 0.0006% of hospital consultations (71 in total) were for actinomycosis in England between 2002 and 2003.[w3] The incidence of all forms of actinomycosis is thought to have declined in recent years, especially in developed countries as a result of better oral hygiene and susceptibility to a broad range of antibiotics.[1]

A large case series from 1975 found that men were three times more likely to be infected than women,[5] although pelvic actinomycosis mainly affects women who have intrauterine contraceptive devices (IUDs).[6] The authors of another case series suggested that the higher prevalence in men might be explained by poorer oral hygiene and higher rates of oral trauma in men from fistfights, although this has not been substantiated.[7] A 2005 review noted that although actinomycosis affects immunocompromised people, most reported cases have been in immunocompetent people.[8] The components of the immune response that are crucial in the control of actinomycosis and the specific effects (if any) of immunocompromise on the incidence of infection are unclear.[1] Box 1 summarises the risk factors associated with actinomycosis.

SOURCES AND SELECTION CRITERIA

We searched PubMed, Web of Science, and the Cochrane Library up to December 2010. We analysed randomised controlled trials, prospective analytical and retrospective studies, review articles, and case reports.

Box 1 | Risk factors associated with the acquisition of actinomyces

- Age 20-60 years[9]
- Male sex (except for pelvic actinomycosis, which mainly affects women)[5 6]
- Diabetes[w43 w44]
- **Immunosuppression**
- Steroids[w45]
- Bisphosphonates[w46]
- Leukaemia with chemotherapy[w47 w48]
- HIV[w49]
- Lung and renal transplant receipt[w50 w51]
- Alcoholism[w13 w52]
- Local tissue damage caused by trauma, recent surgery, irradiation[10]

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- Managing perioperative risk in patients undergoing elective non-cardiac surgery (*BMJ* 2011;343:d5759)
- Fall assessment in older people (*BMJ* 2011;343:d5153)
- Assessing and helping carers of older people (*BMJ* 2011;343:d5202)
- Depression in older adults (*BMJ* 2011;343:d5210)
- Cognitive assessment of older people (*BMJ* 2011;343:d5042)

SUMMARY POINTS

- Although rare, a high level of clinical suspicion is needed to diagnose and cure actinomycosis in patients with indolent, unresolving, or relapsing chronic inflammatory disease
- Actinomyces are commensals that become pathogenic when the mucosa is breached, and co-infection with other organisms is common
- Disease is defined by anatomical location; orocervicofacial disease is the most common, followed by thoracic and abdominopelvic disease
- A mass characteristically enlarges across tissue planes and local tissue invasion may lead to the formation of sinus tracts that can spontaneously heal and recur
- Actinomycosis often mimics other infections and malignancy—clinically and radiologically
- It is generally treated with long term antibiotics, usually penicillin, but surgery may be needed

How does it present?

Actinomycosis is classified into distinct clinical forms according to the anatomical site infected: orocervicofacial, thoracic, abdominopelvic, central nervous system, musculoskeletal, and disseminated. Of the more than 30 species, *A israelii* is the most common human pathogen and is found in most clinical presentations, but certain species have been linked to particular clinical syndromes. For example, in one study of 1997 cases, *A israelii* and *A gerencseriae* comprised almost 70% of orocervicofacial infections.[11] Less common species include *A naeslundii*, *A odontolyticus*, *A viscosus*, *A meyeri*, *A turicensis*, and *A radingae*.[3 4]

Orocervicofacial actinomycosis is the most common form of the disease and comprises about 50% of all reported cases.[5] It usually follows dental manipulation or trauma to the mouth, although it can arise spontaneously in patients with poor dental hygiene.[w4] Common presenting features include fever and chronic painless or painful soft tissue swelling of the perimandibular region, from which sinus tracts can develop over time.[12] Lesions may develop a firm woody consistency that often leads to a misdiagnosis of malignancy. Regional lymphadenopathy is typically absent until later stages.[8] Infection may also extend into local structures such as bone and muscle. In a retrospective study of 317 patients with cervicofacial actinomycosis, bone infection (periostitis and osteomyelitis) developed in 11.7% of cases.[12] One case study reported involvement of the muscles of mastication, which led to chewing difficulties and trismus.[w5]

Thoracic actinomycosis accounts for 15-20% of cases.[5 13] Infection normally results from aspiration of oropharyngeal secretions, but it can also occur after oesophageal perforation, local spread from cervicofacial or abdominal infection, or from haematogenous spread.[3] A higher incidence has been reported in patients with underlying lung disorders, such as emphysema, chronic bronchitis, and bronchiectasis, but the reported series are small.[10 13] Actinomyces are thought to colonise devitalised tissues, which are common in these conditions,[13] although another study reported that actinomycosis did not seem to be caused by the underlying lung disease.[w6] Diagnosis and treatment can be even more challenging if there is coexistent lung disease such as tuberculosis or malignancy.[w7 w8] Initially the clinical picture may be that of pneumonia with a low grade fever, cough, shortness of breath, and chest pain. However, there is usually a longer history of illness and associated weight loss and haemoptysis.[14]

Complications such as empyema necessitans (a rare complication of empyema in which the pleural infection spreads to affect the soft tissues of the chest wall),[w9] pleural effusion,[w10] mediastinal invasion,[w11] and rib destruction[w12] have been reported. Mediastinal disease can progress into the heart, with the most common presentation here being pericarditis.[w13 w14] Myocarditis and endocarditis occur less often, either via extension from the pericardium or by haematogenous spread.[w15 w16]

Abdominopelvic actinomycosis makes up about 20% of cases.[5] Patients who have had acute appendicitis, particularly with perforation, account for most (65%) cases and can present with a right iliac fossa mass.[w17 w18] Other predisposing factors include gastrointestinal perforation, previous surgery, neoplasia, and foreign bodies in the gastrointestinal tract or genitourinary tract, with or without erosion through the mucosal barrier.[15] These infections can be difficult to diagnose because patients may present with non-specific symptoms such as fever, weight loss, and abdominal pain. There may not always be a palpable mass,[16 w19] and fewer than 10% of cases are diagnosed preoperatively.[w20] Infection can spread directly into neighbouring tissues, and sinus tracts may form into the abdominal wall or the perianal region.[1]

Although abdominal disease can spread directly into the pelvis, pelvic actinomycosis is predominantly associated with intrauterine contraceptive devices.[6 16] Patients usually present with a history of prolonged use (>2 years) and symptoms of fever, vaginal discharge, pelvic or abdominal pain, and weight loss.[6 17 18] Although the use of such devices is strongly correlated with intra-abdominal actinomycosis, the duration of use needed to increase the risk of developing infection is not known.[16]

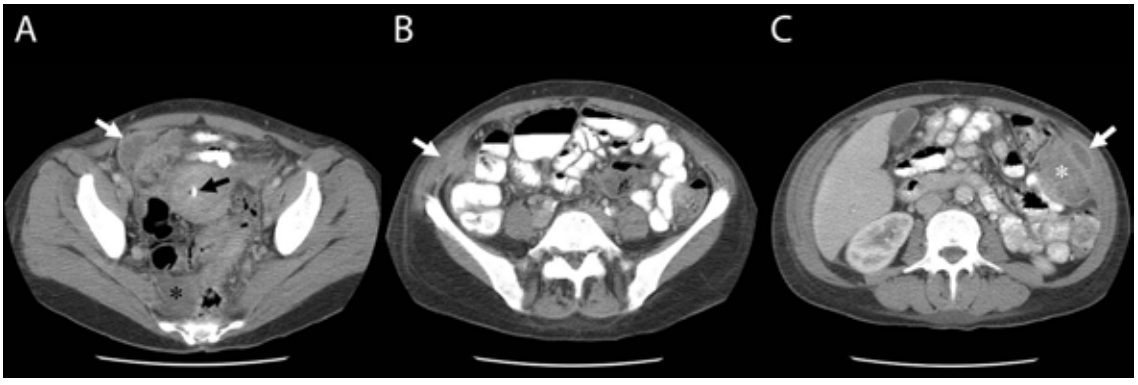

Fig 1 | Axial computed tomograms with oral and intravenous contrast medium from the abdomen and pelvis of the same patient. (A) A low density collection with rim enhancement, consistent with an abscess, is seen in the right iliac fossa (white arrow); free fluid is seen in the presacral region of the pelvis (black asterisk); an intrauterine device is also present within the endometrial cavity of the uterus (black arrow). (B) Inflammatory thickening of the anterior abdominal wall musculature and underlying intraperitoneal fat is seen in the right iliac fossa (white arrow); compare this with normal appearances on the left. (C) A small rim enhancing collection is seen within the anterior abdominal wall musculature of the left upper quadrant consistent with another abscess (white arrow) and a bulky region of phlegmonous change in the underlying intraperitoneal fat (white asterisk). Although these features are non-specific, the constellation of inflammation and abscess formation across tissue planes in the presence of an intrauterine device is strongly suggestive of actinomycosis infection

Differential diagnoses of actinomycosis

Type of actinomycosis	Differential diagnosis
Orocervicofacial[9]	Abscess by other typical bacteria, cyst, neoplasm, tuberculosis (scrofula), nocardiosis
Thoracic[1 9]	Tuberculosis, lymphoma, bronchogenic carcinoma, mesothelioma, blastomycosis, nocardiosis, histoplasmosis, cryptococcosis, pulmonary infarction, abscess or pneumonia by more typical pathogens
Abdominopelvic[3 16]	Intestinal tuberculosis, nocardiosis, tubo-ovarian or pelvic abscess, carcinoma, lymphoma, chronic appendicitis, regional enteritis, inflammatory bowel disease, diverticulitis, endometriosis, pelvic inflammatory disease
Central nervous system[1 3]	Infection or abscess by pyogenic bacteria, tuberculosis, nocardiosis, neoplasm, colloid or dermoid cysts, cholesteatoma, aneurysm of the basilar artery

Box 2 | Clinical "warning signs" of actinomycosis[1]

- Indolent course
- Chronicity
- Mass-like features
- Development of sinus tracts (which can heal and re-form)
- Progression through tissue planes
- Refractory or relapsing infection after short course of antibiotics

Rare sites of actinomycosis include the central nervous system, bones, muscle tissue, and prosthetic joints. Central nervous system infection usually arises from haematogenous spread or direct extension of orocervicofacial infection. In one study, the distribution of presentations of 70 cases of central nervous system disease was: brain abscess (67%), meningitis or meningoencephalitis (13%), actinomycoma (7%), subdural empyema (6%), and epidural abscess (6%).[19] For non-meningitic infection, the clinical picture was usually that of a space occupying lesion with symptoms of headache and focal neurological signs related to the anatomical site of disease.

Musculoskeletal infections are usually caused by spread from adjacent soft tissue (75% of cases), but can also be from local trauma (19%) or haematogenous spread (3%).[20] The facial bones, especially the mandible, are the most common sites of bone disease.[12] Actinomycotic infections of hip and knee prostheses have been described, with early presentation suggesting introduction of the organism perioperatively, and late presentation usually indicating haematogenous spread from an extra-articular site.[w21 w22]

Although all species of actinomyces are capable of haematogenous spread, disseminated actinomycosis is exceedingly rare since the development of antibiotics. *A meyeri*, *A israeli*, and *A odontolyticus* are most commonly associated with this clinical syndrome.[21]

How is actinomycosis diagnosed?

Box 2 lists the clinical "warning signs" for actinomycosis; the table outlines important differential diagnoses to consider in each of the clinical syndromes. Making the diagnosis is difficult—a definitive diagnosis depends on isolating the organism from a clinical specimen.

Blood tests

Findings are non-specific. There may be evidence of anaemia, mild leucocytosis, raised erythrocyte sedimentation rate, and raised C reactive protein values.[2 6 13] Alkaline phosphatase concentration may be raised in hepatic actinomycosis.[w23]

Imaging

In the early stages of infection, imaging features are usually non-specific and non-diagnostic, and they may be similar to findings for other local inflammatory or neoplastic processes (especially tumours in the lung).[13] Cross sectional imaging with computed tomography or magnetic resonance imaging usually yields non-specific features of an abscess or phlegmon but does provide accurate anatomical localisation, which can aid tissue sampling (fig 1). Unlike most other infections, local or regional lymphadenopathy is rarely a feature. In the later stages of infection, there may be evidence of infiltration of surrounding tissues across tissue planes, with sinus tract formation that is characteristic of, but not specific to, actinomycosis.[22-24]

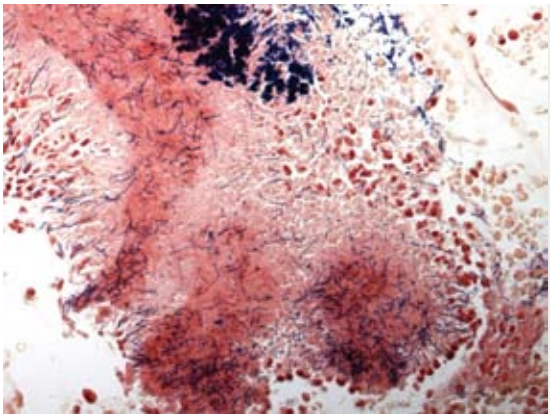

Fig 2 | Gram positive filamentous actinomyces (Gram stain, original magnification ×40)

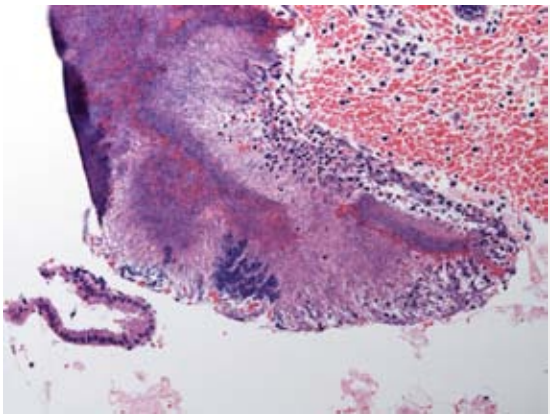

Fig 3 | Sulphur granules showing dense aggregate of Gram positive filamentous non-spore forming actinomyces with adjacent neutrophilic cell infiltrate. The filaments are surrounded by eosinophilic proteinaceous material, which represents host reaction (Splendore-Hoeppli phenomenon) (haematoxylin-eosin stain, original magnification ×20)

Histopathology

Demonstration of Gram positive filamentous organisms and sulphur granules on histological examination is strongly supportive of a diagnosis of actinomycosis (figs 2 and 3). Sulphur granules are colonies of organisms that appear as round or oval basophilic masses with eosinophilic terminal "clubs" on staining with haematoxylin-eosin. Although the presence of sulphur granules is helpful in making the diagnosis, they are not always recovered in culture confirmed cases of actinomycosis.[3] In one series of 181 cases of actinomycosis, the average number per specimen examined was seven, but one to three granules were present in 56% of the cases, and only one granule was found in 26%. None was seen in seven cases in which actinomyces had been cultured.[10] Furthermore, granules are not specific to actinomycosis because they are seen in other diseases, including nocardiosis, chromomycosis, and botryomycosis.[3] Special stains including Gram, Gomori methanamine-silver, and Giemsa are needed

to demonstrate the Gram positive filamentous branching bacteria at the periphery of the grains.[1] A species specific fluorescent antibody allows rapid identification by direct staining, even after fixation in formalin. One small study of cervicofacial actinomycosis showed good correlation between conventional staining and *A israeli* conjugate staining of tissue sections. This technique has the advantage of specificity and is useful in mixed infections.[w24]

Microbiology

Direct isolation of the organism from a clinical specimen or from sulphur granules is necessary for a definitive diagnosis. However, the failure rate of isolation is high (>50%) for various reasons, including previous antibiotic treatment, overgrowth of concomitant organisms, or inadequate methodology.[7] The most appropriate clinical specimens are samples of pus, tissue, or sulphur granules. Swabs are not ideal because, although they can be cultured, the initial sample cannot be analysed with microscopy—a Gram stain of the specimen is usually more sensitive than culture, particularly if the patient has received antibiotics.[1] Avoid antibiotic treatment before obtaining the specimen and transport it as quickly as possible to the laboratory.[9] Depending on the site of infection, tissue may be obtained via image guided (computed tomography or ultrasound) or direct surgical sampling.[25 w25-w27] Clinicians should tell the laboratory to expect the specimen and specifically request actinomycosis culture on the laboratory request form to ensure that prolonged culture on appropriate media is performed.

Actinomyces are slow growing organisms that can be cultured on selective agar medium at 37°C anaerobically for up to three weeks. In a general clinical microbiology laboratory, the organism is identified by colony morphology on agar and biochemical profiling.[1] Commercial biochemical kits have made identification easier and quicker, although one study reported the accuracy of kits to be poor (below 60%) compared with conventional biochemical tests.[26] Serological assays have been developed but sensitivity and specificity need to be improved before they become clinically useful.[1] New molecular genetic methods, such as polymerase chain reaction,[w28] 16s rRNA sequencing,[w28] fluorescence in situ hybridisation,[w28] and mass spectrometry,[w29] are available for more rapid and accurate identification in reference or research laboratories. The 16s rRNA sequencing is currently the preferred method of detecting actinomyces in clinical material in UK reference laboratories.

How is actinomycosis managed?

Clinical experience has shown that actinomycosis can be cured by high doses of antibiotics, such as penicillin for six to 12 months.[1 9] However, the modern approach to treatment is more individualised, and the exact antibiotic regimen depends on the site of infection, severity of disease, and the patient's response to treatment. We would suggest discussing the patient with the microbiology or infectious diseases team to ensure that treatment is appropriate. Patients are regularly monitored to assess their clinical and radiological progress and ultimately to confirm resolution of the disease.

Which antibiotics can be used to treat actinomycosis?

Historically, patients with all forms of actinomycosis have been treated with high doses (18-24 million units a day) of intravenous penicillin G over two to six weeks, followed by oral penicillin V at a dose of 2-4 g/day for six to 12 months.[1 9] The risk of actinomyces developing penicillin resistance is low.[9] In vitro studies have reported that actinomyces are susceptible to a wide range of antimicrobial agents. A UK study of 87 clinical isolates of actinomyces showed that most were susceptible to β lactams (including benzylpenicillin, amoxicillin, ceftriaxone, meropenem, and piperacillin-tazobactam), doxycycline, clindamycin, erythromycin, and clarithromycin. Species identification was found to be crucial because of resistance to some antibiotics.[27] These findings were supported by another study in Denmark in 2009.[28] These studies also found that many species of actinomyces were susceptible to newer antimicrobial agents such as linezolid[27 28] and tigecycline,[28] whereas fluoroquinolones (such as ciprofloxacin and moxifloxacin) and tetracyclines performed poorly.[27 28] However, tetracyclines have been widely used clinically with success,[1 7] and although data on quinolones are limited, there have been anecdotal reports of cure with these antibiotics.[w30 w31]

Doxycycline, minocycline, clindamycin, and erythromycin are suitable for patients who are allergic to penicillin.[1 5 29-31] Erythromycin is a safe option for pregnant patients.[1]

Little clinical evidence is available on the newer β lactam agents except for reports of infections treated successfully with ceftriaxone,[w32] piperacillin-tazobactam,[w33] imipenem,[w34] and meropenem.[w35] Antibiotics with no in vitro activity against actinomyces include metronidazole, aminoglycosides, oxacillin, dicloxacillin, and cefalexin; these antibiotics should not be used alone as therapeutic options.[w36]

What are the appropriate choices for initial antibiotic treatment?

The therapeutic regimen should take into account the site of infection and the other pathogens that may also be present. Although the role of these co-isolates in the pathogenesis of actinomycosis is unclear, many of the organisms are pathogens in their own right, so the initial phase of treatment should cover other bacteria found at the site of infection. A first line regimen might consist of a β lactam and a β lactamase inhibitor such as clavulanate or tazobactam, which offers additional cover against potential β lactamase producers such as *S aureus*, Gram negative anaerobes, and—in abdominal actinomycosis—Enterobacteriaceae.[9 27] In abdominal actinomycosis, a possible treatment of choice is a combination of amoxicillin and clavulanic acid with metronidazole (or clindamycin) for strict anaerobes plus an aminoglycoside, such gentamicin, for resistant Enterobacteriaceae. In such clinical settings piperacillin-tazobactam or a carbapenem (imipenem or meropenem) may be a suitable alternative.[27]

When should surgery be considered?

Although antibiotics are the cornerstone of treatment for actinomycosis, surgical resection of infected tissue may also be necessary in some cases, especially if exten-

ADDITIONAL EDUCATIONAL RESOURCES

Resources for healthcare professionals

Russo TA. Agents of actinomycosis. In: Mandell GL, Bennett JE, Dolin R, eds. *Principles and practice of infectious diseases*. 7th ed. Elsevier Churchill Livingstone, 2010:3209-19

Smego RA Jr, Foglia G. Actinomycosis. *Clin Infect Dis* 1998;26:1255-61; quiz 62-3.

Bonacho I, Pita S, Gomez-Besteiro MI. The importance of the removal of the intrauterine device in genital colonization by actinomyces. *Gynecol Obstet Invest* 2001;52:119-23

Resources for patients

NHS choices (www.nhs.uk/conditions/Actinomycosis/Pages/Introduction.aspx)—Information on all types of actinomycoses; inludes video material

Patient UK (www.patient.co.uk/doctor/Actinomycosis.htm)—Information on the causes, presentation, and management of actinomycosis

QUESTIONS FOR FUTURE RESEARCH

- What is the true burden of disease in different epidemiological settings?
- What are the exact associations between actinomyces and the coexisting bacteria with respect to the pathogenesis of disease, and what are the implications for treatment?
- What effect (if any) do various forms of immunosuppression have on the risk of actinomycosis?
- What are the comparative clinical efficacies of the different antimicrobial agents used in actinomycosis?
- Could treatment regimens be improved and, in particular, shortened?
- Can newer techniques (such as 16s rRNA sequencing) improve diagnosis and outcome in routine clinical practice?

TIPS FOR NON-SPECIALISTS

- If the patient is clinically stable, to ensure a definitive diagnosis avoid treating with antibiotics until a clinical specimen can be obtained
- If a sample of pus or sulphur granules is obtained from a sinus or abscess, ask specifically for actinomyces culture on the laboratory request form; avoid using a swab to obtain the sample
- Ensure the clinical specimen arrives quickly at the microbiology laboratory and warn the laboratory of its impending arrival
- Regular long term follow-up of the patient is important during extended antibiotic treatment to ascertain adherence and to assess for clearance of infection

sive necrotic tissue, sinus tracts, or fistulas are present. It may also be needed if malignancy cannot be excluded or if large abscesses or empyemas cannot be drained by percutaneous aspiration.[9] The need for surgery must be assessed on an individual basis. Surgery may be a valid option for patients who do not respond to medical treatment. A retrospective analysis of patients with thoracic actinomycosis showed that surgery cleared the disease in five patients who responded unfavourably to initial antibiotics.[25] Surgery may also be used to control symptoms, as in the control of haemoptysis in thoracic actinomycosis.[w37]

What is the optimal duration of treatment?

The duration of antibiotic treatment will depend on the initial burden of disease, the performance of resectional surgery, and the patient's response to treatment.[9] The traditional recommendation of six to 12 months may not be needed for all patients. Several studies have reported using shorter courses of antibiotics for actinomycosis. Orocervicofacial disease has been cured after short courses of two to six weeks of antibiotics (oral and intravenous) combined with surgical drainage.[32]

Thoracic actinomycosis can also be treated with relatively brief courses of treatment. A survey described 19 patients in whom thoracic actinomycosis was cured with a median duration of six weeks of antibiotics (range, one week to six months). Surgical resection was performed in seven patients. Another study of 16 patients with thoracic actinomycosis reported cure with a median duration of two weeks of intravenous penicillin and three months of oral penicillin. Nine of these patients underwent surgical debulking.[32]

Studies have also shown that pelvic disease can be cured by shorter courses of antibiotics. One retrospective analysis demonstrated cure after surgical removal of the lesion and three months of antibiotics.[w38] Cure has also been reported after only one to two months of antibiotics.[w39 w40] If short term antibiotic treatment is attempted, the clinical and radiological response must be closely monitored.[32]

What is the treatment for immunocompromised patients?

Antibiotic regimens used to treat actinomycosis in immunocompetent patients are also suitable for immunocompromised patients.[1] However, there have been reports of refractory responses to treatment in certain settings, such as HIV, and it would be prudent to discuss the patient with a microbiologist or infectious diseases specialist.[w41]

What should happen to IUDs in pelvic or abdominal actinomycosis?

We recommend that IUDs are removed in patients with pelvic or abdominal actinomycosis. A randomised controlled trial showed that in addition to treatment with antibiotics, removal of the IUD was effective in eliminating genital actinomyces colonisation.[33] Furthermore, one report has recommended the removal of IUDs in patients with abdominal actinomycosis associated with an IUD.[w42]

What is the prognosis of actinomycosis?

Reports of mortality range from 0% to 28% depending on the site of infection, the time to diagnosis, and the time to the start of appropriate treatment, with the highest mortality seen in central nervous system disease.[2] It is therefore crucial to make an early and accurate diagnosis of actinomycosis.

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ANSWERS TO ENDGAMES, p 801. For long answers go to the Education channel on bmj.com

STATISTICAL QUESTION

Screening tests and indices of performance: effects of prevalence

The positive and negative predictive values (answers *c* and *d*) would change, while the sensitivity and specificity (answers *a* and *b*) would remain unaffected.

ANATOMY QUIZ

Magnetic resonance image of the heart

A Interatrial septum
B Coronary sulcus
C Pericardium
D Left circumflex artery
E Small cardiac vein

ON EXAMINATION QUESTION

Eczema

Answer C is correct.

CASE REPORT

Abdominal pain

1 Differential diagnoses include:
- Gynaecological causes, such as mittelschmerz, menarche, dysmenorrhoea, and ruptured ovarian cyst
- Gastrointestinal causes, such as bowel obstruction, inflammatory bowel disease, pancreatitis
- Metabolic causes such as diabetic ketoacidosis and porphyria.

But the most common cause of abdominal pain, specifically in the right iliac fossa, is acute appendicitis.

2 When it is difficult to reach a clinical diagnosis, ultrasound or computed tomography scanning can be useful. Several studies have shown that this type of imaging is helpful, with computed tomography having greater sensitivity than ultrasound. Results must be interpreted with knowledge of the clinical presentation.

3 The Alvarado scoring system first introduced in 1986 can be used to help diagnose appendicitis.

4 Pending a certain diagnosis, the patient should receive adequate analgesia, anti-emetics, and intravenous fluids. Once a diagnosis of appendicitis is made, the management is usually appendicectomy, except in specific circumstances, such as delayed presentation with appendicular mass, when immediate surgery is best avoided.