

REVIEW

Fungal arthritis

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There are 50 000–200 000 species of fungi, but only about 100 of these cause infectious diseases (mycoses) in humans.¹ Fungal infections are not readily recognised, do not advertise their presence in a characteristic fashion, and the causative organism is generally not easy to demonstrate in tissue.² Musculoskeletal infection by fungi was once rare, but its incidence has increased in the past few years. Although healthy subjects may host fungal diseases, various predisposing factors that depress the immune system have been implicated in most patients developing fungal infections or fungal arthritis, or both.³ Alcoholism, cirrhosis, diabetes, tuberculosis, cancer, prematurity, treatment with corticosteroids, cytotoxic drugs, prolonged use of intravenous antibiotics, intravenous drug abuse, granulocytopenia, and marrow hyperplasia are among the predisposing factors.

Fungal arthritis usually follows a chronic indolent course of several months that leads to delays in diagnosis and to inappropriate treatment such as intra-articular and systemic steroids. Consequently, it is important to know the epidemiology and extra-articular manifestations of fungal disease to be aware of the possibility of musculoskeletal infection and to establish an appropriate treatment. The table gives the main characteristics of fungal arthritis.

Candidiasis

Candida organisms are normal commensals of humans and are commonly found on diseased skin, the gastrointestinal tract, expectorated sputum, the female genital tract, and in urine of patients with indwelling Foley catheters.⁴ Most candida infections are of endogenous origin, but human to human or animal to human transmission is possible, which is a unique property among the mycoses affecting humans. There is also evidence that candida infection can be acquired from the hospital environment.

Fungal arthritis: demographic and clinical characteristics

Worldwide distribution in most instances
Affects neonates, old, or immunocompromised hosts
Prevalence is variable, ranging from 0.4 to 20% of disseminated mycosis
More common in men, and may be an occupational hazard
Joint disease occurs by contiguous or haematogenous spread
Usually monoarthritis or oligoarthritis, with the knee joint most commonly affected
Systemic disease often absent
Pulmonary and cutaneous disease are the extra-articular manifestations most often present
Diagnosis is based on direct visualisation of the organism or synovial fluid and membrane cultures, or both
Combined medical (antimycotic) and surgical treatment often necessary

Candida infections, both focal and generalised, have been increasing rapidly in recent years. These organisms become pathogens when there is an interruption of the normal defence mechanisms of the host by naturally occurring or iatrogenic factors.⁴ Candida species are the most common fungi associated with opportunistic infections.³

Septic arthritis caused by candida species is uncommon and its true incidence is unknown.⁵ It can be divided into two clinical syndromes. The first is an isolated monoarthritis caused by the direct intra-articular inoculation of fungi that inhabit the skin. The second is the development of a monoarthritis or pauciarthritis as a complication of haematogenously disseminated candidiasis.

The first manner of introducing the organism to the joint is by injection. The common denominator is repeated aspiration, usually with injection of corticosteroids, of a previously damaged knee joint.^{5,6} This type of arthritis is extremely rare and only eight cases have been described. The diagnosis is by means of a positive culture or biopsy sample. Synovial fluid white blood counts range from 9 to 43 × 10⁹/l with a predominance of polymorphonuclear leucocytes. Uncommon species of candida have been isolated from joints: *C guilliermondi* twice, *C parapsilosis* four times, and unspecified candida species twice. The onset of this type of arthritis is insidious and the course indolent, chronic, and relatively benign. The patients are afebrile and have normal blood cell counts.

Candida may also enter the joint by contamination during surgery.^{7,8} Eleven episodes of fungal arthritis by candida complicating knee, hip, and shoulder reconstructive arthroplasty have been reported in nine patients. All patients had only pain with a limited range of motion and swelling, and there was no evidence of systemic disease. The onset of symptoms occurred as late as two years after the initial surgery with an average interval of 14 months. All peripheral white blood cell counts reported were normal. The white blood cell counts in joint fluid ranged from 4 to 15 × 10⁹/l. The cultures yielded *C albicans* in two patients, *C tropicalis* in three, *C parapsilosis* in three, and *C glabrata* in one. Treatment requires the removal of the prosthetic components with debridement. Although infection is the most common cause of biological failure of joint arthroplasty, fungal infection in this setting remains extremely rare.

Arthritis complicating haematogenously disseminated candidiasis occurs in patients with predisposing factors.⁵ Patients are sick and the inflammation usually occurs in normal joints.

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Neonates are the first group of patients in whom haematogenously originated candida arthritis can occur.⁵⁻⁹ The illness is a hospital acquired disease of sick children with underlying diseases such as the respiratory distress syndrome, and gastrointestinal defects. *C albicans*, which is responsible for more than 80% of the reported cases, and *C tropicalis* are the species responsible for this disease. Arthritis is usually present with accompanying metaphyseal osteomyelitis. Bone infection might originate from the infected synovium or via the metaphyseal vessels. Polyarthritis occurs in most patients and the knee is the joint most often affected. Physical examination shows a febrile child with swollen and tender joints. Radiographs show joint effusion, dislocation of the joint in some instances, irregularities and punched out lesions at the metaphysis, and, less commonly, periosteal reactions.

Diagnosis is achieved by isolating the organism by culture of the aspirated joint fluid or bone. Treatment against candida is effective and reduced joint function occurs in only a small percentage of cases.

Arthritis originated by haematogenous dissemination beyond the neonatal period is usually a complication of disseminated candidiasis in patients with serious underlying disorders or intravenous drug abusers.⁵⁻¹⁰⁻¹¹ *C albicans* is again the causative organism in about 80% of cases, and *C tropicalis* is responsible for most of the remaining cases. Isolated cases of knee arthritis caused by *C parapsilosis*,¹² *C krusei*,¹³ and *C zeylanoides*¹⁴ have been reported.

Two distinct clinical presentations can be observed: (a) acute onset of constitutional and synovial symptoms (about two thirds of patients), with the aetiological diagnosis established within the first week, and (b) indolent presentation, with mild systemic and arthritic symptoms, and delay in the diagnosis for months or years, including some cases diagnosed at necropsy. The knee is affected in most cases, though any other peripheral joint or the spine can also be affected. Most cases are monoarticular, but polyarticular presentation is common (about 37%). Osteomyelitis is often present (70-85%).¹⁵ The organisms spread to the bone from the affected joint, which is different from other fungal diseases such as coccidioidomycosis, in which osteomyelitis usually precedes arthritis. Infection of the olecranon¹⁶ and popliteal¹⁷ bursae by *C tropicalis* has also been reported.

Synovial fluid shows polymorphonuclear leucocytosis between 7.5 and $151 \times 10^9/l$.⁹ Candida blastospores are rarely seen in Gram stains. The diagnosis is achieved by culture of synovial fluid or synovial biopsy specimens. Synovial effusions and changes consistent with osteomyelitis, without osteopenia, are the usual radiographic abnormalities seen. Scanning with gallium and technetium should be performed when there is pain in the musculoskeletal system in patients predisposed to candida infections.⁵ Positive scans will point to the areas requiring a biopsy sample to be taken. The macroscopic appearance of the synovium is of a boggy, thickened membrane that resembles a typical 'pannus' in more advanced cases.⁹

Microscopically, the synovium shows a thickened membrane with non-specific mononuclear cell infiltration. Isolated synovial fluid lymphocytes show greater stimulation to candida antigens than peripheral blood lymphocytes, and CD4 positive T lymphocyte clones with specificity for candida antigens have been characterised and further propagated in vitro.¹⁸

The use of amphotericin B, either alone or in combination with joint drainage, is associated with clinical and mycological cure in 90% of patients.⁹ Amphotericin B is used intravenously at dosages of 0.3-0.5 mg/kg/day.⁵ A total dose of 1-3 g during a period of six to ten weeks is given, although cures have been obtained with lower doses. Amphotericin B can also be used in combination with 5-fluorocytosine, which seems to have a synergistic interaction with the former. The latter should never be used alone because of the emergence of resistance. 5-Fluorocytosine is available only for treatment by mouth and it is given at doses of 150 mg/kg/day divided into four doses. Intra-articular amphotericin B is a useful adjunctive treatment in infections restricted to the joint capsule and not disseminated, as in pyarthrosis following direct inoculation of candida,⁶⁻⁹ as well as in haematogenously spread infections that have not responded well to systemic treatment.⁹ Other treatment options include ketoconazole and fluconazole.⁵⁻⁶⁻¹⁹

Patients with HIV infection deserve special consideration because, in spite of the profound state of immunodeficiency present, only isolated cases of septic arthritis have been reported.²⁰ Among these cases, candida arthritis is rare. Arthritis and osteomyelitis have been reported in the sternoclavicular joint,²¹ and in the costosternal and hip joints²² of HIV infected intravenous drug abusers. The reported patients had clinical features similar to those previously described in skeletal infections of intravenous drug abusers not infected with HIV. Cases of candida arthritis in other risk groups for HIV infection, such as homosexuals, have not yet been reported. Consequently, the presence of candida arthritis in HIV infected patients seems to be related to drug abuse more than to HIV infection itself.

Experimentally induced candida arthritis in rabbits²³ and rats²⁴ has some similarities to candida arthritis in humans.

Coccidioidosis

Coccidioides immitis is a dimorphic fungus that inhabits soils of desert zones such as the southwestern United States, northern Mexico, and parts of Central and South America.²⁵⁻²⁶ The infection begins after inhalation of the infectious units, arthrospores. This primary pulmonary infection is asymptomatic in 60% of cases and in only 1% does dissemination occur with extension to meninges, skin, lymph nodes, subcutaneous tissue, bones, and joints.²⁷⁻²⁸ In addition to the known predisposing factors, certain ethnic groups such as Filipino and African Americans appear to be at greater risk.²⁹⁻³²

Serological findings are of help in diagnosis

and prognosis. Serum, pleural, peritoneal, and joint fluids can be tested to detect antibodies. Spherule derived antigens (spherulin) are used for complement fixation tests and have great sensitivity, but can cross react with other fungi. IgM antibodies are of value in acute disease, reaching maximum titres at the third week of illness, and may be the confirmatory test for an early acute coccidioidal infection.³³ IgG antibodies develop later, but are more persistent than IgM. There is a correlation between complement fixation titres in serum samples and the severity of coccidioidal disease; titres greater than 1/16 may indicate disseminated disease, and titres greater than 1/128 are associated with bone and joint disease. Negative serological findings with positive histopathological findings are rare. Coccidioidal tests are highly sensitive, and in a severely immunocompromised host the potential for serological failure is only between 20 and 25%.^{34 35} A positive complement fixation result at any titre in synovial fluid supports a diagnosis of coccidioidal arthritis. A positive result in a skin test implies a delayed cutaneous hypersensitivity reaction (with current or previous infection) and the results are apparent within three days to three weeks after the onset of symptoms. A negative skin test does not rule out coccidioidomycosis, and it may be positive in up to 80% of cases of coccidioidal arthritis.

Skeletal manifestations associated with coccidioidomycosis include a chronic granulomatous process in bones, joints, and periarticular structures, and a benign and acute articular process known as 'valley fever' or 'desert rheumatism'.³⁶ The latter is a hypersensitivity syndrome that may occur during primary infection in 20% of cases (eight to 15 days after the onset); accompanying non-specific symptoms such as fever, general aches, sore throat, and mild cough, in addition to peripheral eosinophilia, erythema nodosum, and erythema multiforme, arthralgias, arthritis, and conjunctivitis may be seen. Acute arthritis develops in a third of patients. It is polyarticular, usually migratory, without effusions, and the joints are tender to pressure and painful on motion. It may affect any joint, but most often the ankles and knees, and there is a remission after two to four weeks without residual damage.^{37 38}

Musculoskeletal manifestations can also be seen during the disseminated form in 10–50% of cases.³⁰ Coccidioidal arthritis may be suspected when a patient has chronic progressive mono- or polyarthritis and a history of being in an endemic zone. A history of pulmonary disease or abnormal chest radiographs, or both, may not be apparent. Arthritis may begin in the early stages as intermittent, painful swelling of one joint and, later in the course, it may present with large effusions, thickened synovium, nodular lesions in periarticular skin, and swelling with draining sinuses. Joints may be affected primarily by haematogenous spread or, in most cases, by direct extension from adjacent areas of bony disease. Weight bearing joints are often involved and knees are affected in 50–70% of cases, but any joint may be affected. Osteomyelitis of spine is common, and tenosynovitis,

usually affecting the hands, may also be present. Fever may be the only symptom in approximately 90% of patients. The interval between the onset of symptoms and diagnosis ranges from four weeks to many years, with a mean of 4.5 years. Most patients are men, not white, and with a mean age of 36 years.^{30 39 40} Synovial fluid is turbid with decreased viscosity. Leucocyte counts are moderately high and lymphocytes predominate. High protein levels and normal blood/synovial glucose ratios are found. Fungal cultures may be negative. Histopathological findings include villonodular synovitis or typical pannus formation with non-caseating granulomas, and spherules containing coccidioidal endospores.

Radiological changes may include synovial effusion, osteopenia, joint space narrowing, bony destruction, and in some instances ankylosis.^{37 41–43} Technetium-99m and gallium-67 bone scans can detect early osseous and soft tissue lesions with higher sensitivity than plain films.⁴⁰

Amphotericin B (total dosage 1–10 g) remains the most effective treatment for severe infection with skeletal disease.^{40 44} In limited cases with monoarticular disease local amphotericin B has been used.⁴⁵ Ketoconazole is the drug of second choice.^{46 47} Open drainage, synovectomy, arthrodesis, and, if all else fails, amputation, should be considered.^{39 40}

Blastomycosis

Blastomycosis, Gilchrist's disease, or North American blastomycosis, is caused by *Blastomyces dermatitidis*, a dimorphic fungus often found in the Mississippi and Ohio river valleys, and in the southeastern United States. Infection also occurs in Canada, Central and South America, and Africa.

Acute infection begins in the lungs, and in most cases is asymptomatic and recognisable only by skin tests. Other cases have symptoms such as a productive cough with mucoid sputum, pleural pain, and benign pulmonary lesions that heal spontaneously. Patients may also have joint and muscle pain, pulmonary densities on radiographs, and budding yeast in the sputum. When the primary lesion becomes progressive, it is clinically similar to tuberculosis, histoplasmosis, or coccidioidomycosis. Cutaneous, bone, and joint disease are the main extrapulmonary manifestations, but widespread infection may extend to any organ.^{48 49} Cutaneous lesions are seen in 80% of extrapulmonary disease; skeletal infection appears in up to 60% of cases.^{50–52} The spine is often affected; the infection begins in the vertebral body and can extend to the disc; paravertebral or psoas abscesses may form. Bone disease can be asymptomatic, or begin acutely with pain, redness, and swelling.⁵¹ It may appear with localised (dactylitis) or diffuse osteomyelitis or periostitis, or both, and the epiphyseal line is commonly affected.⁵² Blastomycotic arthritis, which is usually monoarticular (the knee is the most often affected, followed by the ankle, elbow, wrist, and hand), may occur by spread of adjacent osteomyelitis or by haematogenous

dissemination, and without treatment, polyarticular extension may develop.⁵³ It may have an abrupt onset (only candida arthritis may have this presentation), with significant pain and swelling, constitutional symptoms and signs (fever, weight loss), and synovial fluid with pyogenic-like appearance. Patients often have evidence of pulmonary blastomycosis, and, in a high percentage, cutaneous abscesses, ulcerations, or purulent draining sinus tracts are found concomitantly. Two radiological patterns of bone disease may be seen, one focal without a periosteal reaction in short bones but with a periosteal reaction in long bones, and one diffuse, destructive, and expanding form.⁵⁴

The diagnosis of blastomycotic joint infection requires one or more of direct microscopic evidence of the fungus, culture positivity in synovial fluid, or culture positive material at any other site. Organisms are readily identified in joint fluid.⁵⁵

Treatment with amphotericin B results in a resolution of osteomyelitis and arthritis. 2-Hydroxystilbamidine and ketoconazole have been found to be effective.^{51 53 56} As loculations of purulent fluid are often present, incision and drainage, combined with chemotherapy, are reported to be effective.

Histoplasmosis

Histoplasmosis is a deep mycosis caused by *Histoplasma capsulatum* (African histoplasmosis, found rarely in North or South America, is caused by *H capsulatum* var *duboisii* and has a different clinical spectrum affecting skin and bones), a facultative intracellular parasite.⁵⁷ It is a dimorphic fungus that grows in soil in the mycelial form and produces spores. This worldwide disease, found most commonly in temperate climates, is heavily endemic in the Ohio and Mississippi river valleys, and is rare in Europe and Australia. Inhaled spores attack cells of the reticuloendothelial system and spread to the regional lymph nodes, with granulomatous reaction, necrosis, and then calcification. Most primary infections undergo benign self limited dissemination and are asymptomatic, but heavy infections and infections in infants and young children may produce an acute influenza-like syndrome during the primary acute stage. The host may be affected by reinfection, in which instance acute histoplasmosis or chronic pulmonary and disseminated disease may occur. Disseminated disease occurs in less than 0.1% of infections; one third occurs in children and other cases in immunocompromised hosts.^{58 59} Bones and joints are rarely affected.

The most common rheumatic manifestation occurs during primary infection in the form of a migratory polyarthritic syndrome that may or may not coexist with other hypersensitivity reactions such as erythema nodosum or erythema multiforme, or both, pleuritis, and pericarditis.^{60 61} This syndrome is similar to that seen in primary coccidioidomycosis. The articular disease is self limited and disappears without sequelae. The prevalence of erythema nodosum or erythema multiforme associated with primary histoplasmosis is variable, ranging from 0 to 34%.^{62 63}

Arthritis, tenosynovitis, and osteomyelitis are rare complications of disseminated histoplasmosis. Joint disease is characterised by monoarthritis, with the knees most often affected, and usually associated with underlying immunosuppression, including one reported case associated with AIDS.⁶⁴⁻⁶⁶ Flexor tendon sheaths of the wrist have been affected, and carpal tunnel syndrome can be the initial manifestation.⁶⁷ Radiological changes include cortical subperiosteal thickening, widening of the medullary canal, osteopenia, and epiphyseal bone destruction.⁶⁸ Multiple punched out lesions are common in *H duboisii* infection; destructive joint lesions, erosions, sclerosis, and joint space narrowing can occur.^{69 70} Diagnosis is based on the detection of the organism in tissues or exudates. Detection of the organism is possible in only 70% of cases. Complement fixation antibodies to histoplasmin and histoplasma yeast antigens become positive at two to three weeks and are an important diagnostic test. It may produce false positive results in titres of less than 1/16 in about five to 15% of serum samples from patients in endemic areas.⁷¹ Complement fixation titres of 1/32 or greater have diagnostic significance (most instances of false positives have been reported with radioimmunoassays). The histoplasmin skin test becomes positive two weeks after infection, does not discriminate between past or present infection, is positive only in 50% of cases of disseminated disease, and may stimulate antibody formation. For these reasons, the skin test is used primarily for epidemiological studies. In patients with disseminated disease with the musculoskeletal system affected, amphotericin B, with or without surgery, is the treatment of choice. Ketoconazole may also be used with some success.

Sporotrichosis

Sporotrichosis is caused by *Sporothrix schenckii*, a dimorphic fungus with low virulence that is saprophytic in nature, and was first reported by Schenck in 1898. De Beurmann *et al* in 1909 described gummatous intraosseous lesions.⁷² It is almost always a lymphocutaneous disease; infections usually occur after cutaneous inoculation during outdoor work such as farming. Less often, infection may occur by the inhalation of spores that produce a chronic granulomatous pneumonitis, especially over an underlying structural abnormality of the lungs.⁷³ Dissemination is uncommon, but when it occurs, any organ system including the joints can be affected.⁷⁴⁻⁷⁸

Manifestations of sporotrichosis include lymphangitic and fixed cutaneous lesions in 75-80% of cases (cutaneous ulcers and nodules along the course of the lymphatics). Mucocutaneous, extracutaneous, or disseminated and primary pulmonary disease complete the extent of clinical involvement.⁷⁹⁻⁸⁴ Arthritis is usually chronic, mono- or polyarticular, affecting weight bearing joints (the knee most often, but also the wrist and small joints of the hands and feet). Diagnosis is usually delayed (three to 96 months from onset of symptoms).^{80 85} Laboratory data

are non-specific; an increased erythrocyte sedimentation rate is the most common abnormality found. Synovial fluid may be serosanguinolent and inflamed, with low glucose levels. Diagnosis requires synovial fluid or tissue cultures and is often repeated and prolonged.⁸⁵ Skin tests are not useful, but agglutination and immunodiffusion (precipitation) procedures can be used in the diagnosis.⁸⁶ Precipitins can be shown in 70–85% of infected subjects, and latex agglutination in a higher percentage. Higher agglutinin titres are seen in patients with articular disease, and decrease with treatment.

Intravenous amphotericin B at doses of more than 1 g in one course of approximately 12 weeks has been shown to be effective in sporotrichal arthritis, although sometimes more than one course is necessary to eradicate the infection.⁸⁰ Intra-articular amphotericin B and synovectomy are also effective.⁸⁷

Cryptococcosis

Cryptococcus neoformans is a dimorphic encapsulated yeast-like fungus found widely in nature and in most countries of the world in association with pigeon droppings.^{60–88} Cryptococcosis may be acute, subacute, or chronic, and presents as a primary pulmonary infection. Haematogenous dissemination causes multiple extrapulmonary sites, including bone and joints, to be affected. Dissemination can occur in immunocompromised and competent hosts. Cryptococcosis is the next most common fungal pathogen following systemic candidiasis and aspergillosis in immunosuppression associated deep mycoses.

The most common musculoskeletal manifestation is osteomyelitis, which may occur in 5–10% of patients.⁸⁹ It follows a subacute or chronic course with symptoms occurring several weeks to months before diagnosis. All major bones can be affected, and the osseous foci are usually single but may be multiple.^{88–90} The patient experiences pain or swelling, or both, in the affected area. Radiographic features are not specific, but osteolytic lesions predominate.⁶⁰ The organism can be identified by a biopsy.

Arthritis is a rare manifestation of cryptococcosis, and is usually secondary to extension of adjacent osteomyelitis.^{88–91} A history of contact with pigeons is absent in most patients and there is no apparent racial or occupational association.⁸⁸ Approximately half of the patients have a predisposing factor. The most common presentation is monoarthritis, though oligoarthritis and polyarthritis can occur. The knee is the joint most commonly affected, though the elbow, sternoclavicular, sacroiliac, and ankle joints can also be affected. Systemic symptoms such as malaise, weight loss, or low grade fever may be found. Physical examination shows variable effusion with occasional synovial thickening. The course is usually subacute or chronic, with a diagnostic interval ranging from two weeks to eight months. There is often no evidence of infection in another organ system. Laboratory findings are non-specific. Synovial fluid is described as turbid, purulent, and viscous. The leucocyte count ranges from 0.2 to

$19 \times 10^9/l$, with a predominance of mononuclear cells. Radiographic findings consist of synovial effusion and lytic lesions indicative of osteomyelitis in contiguous bone.⁶⁰ Histopathological findings include both acute and chronic synovitis.^{60–88} Cryptococci can be shown with special stains of synovial tissue.⁶⁰ Diagnosis is made by isolation of the organism from biopsy material or synovial fluid.

Combined medical and surgical treatment offers the best results.^{60–88} The combination of intravenous amphotericin B and 5-fluorocytosine by mouth, which have shown in vitro synergy against many cryptococcal strains and an in vivo efficacy in the murine model, provides effective medical treatment.⁶⁰

Aspergillosis

Aspergillus, a dimorphic fungus, is ubiquitous throughout the world and may occasionally cause human infection, most commonly in the immunosuppressed host.⁸⁸ It is a saprophyte in residual cavities or mucus plugs, usually in patients with chronic obstructive pulmonary disease. *Aspergillus fumigatus* is the causative organism in almost all cases, followed by *A. flavus*.

The musculoskeletal system is rarely affected by aspergillus. Osteomyelitis is the most common type of disease. It has been reported mainly in vertebrae, disc spaces, and ribs.^{92–94} The mechanism of infection in children is contiguous spread from a pulmonary infection or from skin, whereas in adults it is haematogenous dissemination.⁹²

Aspergillus arthritis is rare, with only five cases reported.⁸⁸ Four of the patients had a predisposing factor. Nearly all the patients had osteomyelitis of the adjacent bone. The most common symptoms were pain, swelling, and tenderness of the affected joint, and fever, chills, or malaise. Physical examination showed diffuse tenderness, limitation of motion, and synovial effusions.

Mild to moderate leucocytosis and an increased erythrocyte sedimentation rate are found.⁸⁸ The diagnosis is established by isolation of the fungus from the affected tissue or from the synovial fluid. The organism can be seen in histopathological sections of bone and other tissues. Radiographic findings include diffuse soft tissue swelling and typical changes of osteomyelitis. Synovial fluid can be clear, turbid, or serosanguineous.

Treatment includes a combination of surgical debridement and drainage, and intravenous amphotericin B.⁸⁸ Successful treatment with ketoconazole,⁹⁵ and itraconazole⁹⁶ has also been reported.

Miscellaneous

Mycetoma, or 'madura foot', is a chronic, granulomatous, and suppurative infection that follows the integumentary introduction of the infectious organism and progresses locally by destruction of contiguous tissue including muscle, fascia, tendon, bone, and joints.⁹⁷ It

may be caused by a fungus (maduromycosis or eumycetoma), or by actinomyces (actinomycetoma). There are multiple fungi that may cause eumycetoma, and the prevalent organism varies according to the geographical location. The infection begins with the traumatic introduction of the organism, usually in the legs (70% affecting the foot) or hands, though other sites can be affected. The infected foot evolves into a swollen, nodular, discoloured, and deformed extremity with multiple granule draining sinuses. Fascia and bone are affected with bone destruction and evidence of remodelling, and by contiguous spread joints become affected. Secondary bacterial infection with osteomyelitis may occur. Diagnosis is by culture of the granules. Radiological findings are non-specific.⁹⁸ The treatment of choice is complete surgical excision of the affected tissue. Chemotherapy with amphotericin B, griseofulvin, dapson, ketoconazole, and miconazole are reported to be effective.⁹⁹⁻¹⁰¹ A preliminary course of broad spectrum antibiotics is recommended for actinomycetoma.

Petriellidium boydii (*Allescheria boydii*) is a saprophyte isolated from soil, polluted water, sewage, and other outdoor sites.⁸⁸ The organism may cause a broad spectrum of clinical manifestations, but mycetoma (especially in the USA) accounts for about 99% of all infections. Sixteen cases of *P boydii* arthritis have been reported, including those caused by *Scedosporium apiospermum* (asexual expression) of *P boydii* and *Scedosporium inflatum*.^{102 103} The infection is more common in men, in rural areas, and in subjects with a history of previous trauma. Joint pain, swelling, and decreased range of motion are usually present. Systemic symptoms are absent. Monoarthritis affecting the knee is the most common presentation. Oligoarthritis may be seen. Arthritis develops within 10 days to one year after the trauma, suggesting that the articular infection occurs by extension from adjacent tissue. Leucocytosis and an increased erythrocyte sedimentation rate may be found. Radiographic findings consist of osteopenia, soft tissue swelling, and lytic lesions of the articular surfaces. Medical treatment with miconazole, ketoconazole, and intra-articular amphotericin B, as well as surgical treatment, have been used with success.⁸⁸

Septic arthritis caused by *Fusarium solani*, which belongs to the class Deuteromycetes (fungi imperfecti), has been reported.¹⁰⁴ A good clinical response was obtained with amphotericin B and repeated joint aspirations.

Arthritis caused by *Saccharomyces cerevisiae* also occurs.¹⁰⁵ This organism is a beer yeast and may be part of the normal or transient flora of the throat and alimentary tract.⁸⁸

Torulopsis glabrata is a yeast-like fungus closely related to the cryptococcus and candida species. It is a normal resident of human mouth, nose, gastrointestinal tract, and vagina, and is an opportunistic pathogen of low virulence that causes disease in patients admitted to hospital with debilitating diseases.⁸⁸ A case of *T glabrata* arthritis that occurred in the right hip 26 months after joint replacement in a patient with long standing osteoarthritis and morbid obesity

was reported.¹⁰⁶ The prosthesis was removed and a good response to intra-articular amphotericin B was observed.

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