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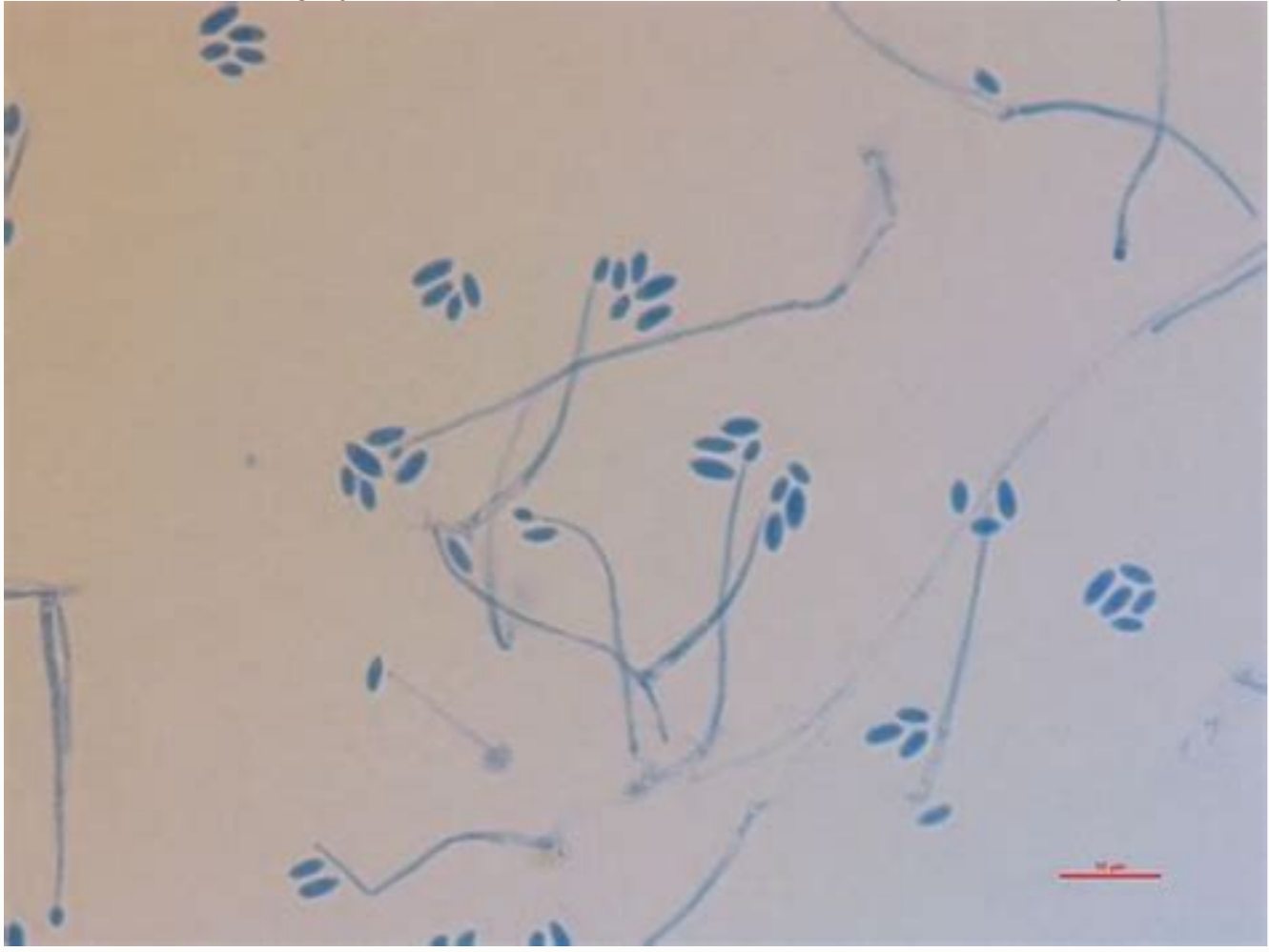


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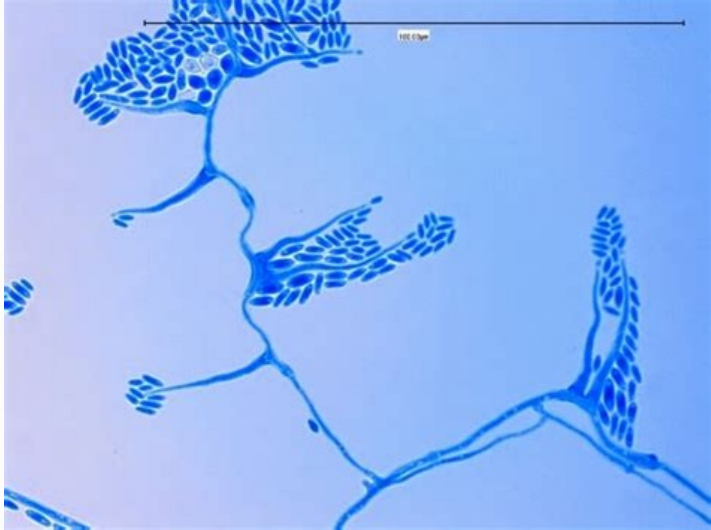
Acremonium spp pdf

Acremonium spp.

Kingdom Fungi Order Hypocreales Phylum Ascomycota Family Hypocreaceae Class Euascomycetes Genus Acremonium The Acremonium genus was formerly known as Cephalosporium. Depending on the different authors, the genus Acremonium currently contains between 20 and 200 recognised named species {814; 813; 3971}. The taxonomic fungal database administered by the International Mycological Association has 205 registered strains of which 197 are named species {3971}. This genus comprises moulds that lack any known sexual state or teleomorph forms and thus belongs to the Fungi Imperfecti group. However, because it possesses structural characteristics similar to those of the Ascomycota group, it is often included in the Ascomycota phylum. Furthermore, some authors have proposed that certain fungi could be sexual stages of different Acremonium species, amongst which include Acanthoitschkea, Albertiniella, Allantonectria, Allescheria, Atkinsonella, Bulbithecium and Bysostilbe {3842}. Habitat/Ecology Acremonium has a world-wide distribution: it is commonly found in the environment in soil and on dead plant material as well as in hay and rotting mushrooms; some species can be also found in foodstuff {813}. The many species of Acremonium are mostly saprophytic and non pathogenic {814; 813}. However, certain species are pathogenic to plants and humans {813; 2114}. The mode of dissemination of wet spores is by insects, water droplets or by wind {2204; 813}. In aerobiological counts, Acremonium is usually present in small concentrations in the outside air and its occurrence may be quite low {1973}. It is reported as one of the less prevalent genera in air samples. Alternatively, some species are widespread indoors {1056; 468}: species reported in the indoor habitat include *A. strictum*, *A. carticola* {1056; 468}, *A. kilianse* and *A. rutilum* {4320}. More details Spores of Acremonium spp. are released in the air as small drops of slime and are thus only discharged into the air in low concentrations {1973}. In northern climates, concentrations in the outdoor air vary seasonally and comprise a small proportion of the natural aerosolised fungal flora. Spore levels of Acremonium appear to be higher in rural as opposed to urban environments {854}. This fungus is isolated in rural environments in cow barns, farm houses and rural outdoors but is rarely observed in urban apartments. One study {854} identified *A. murorum* and *A. strictum* in swineries and grain mills albeit in very low concentrations (less than 1.7% of total isolates). In a study of tap water, Acremonium was found among the highest of total fungal counts {1733}. However, at ambient temperature, none of the fungi isolated could be associated epidemiologically with human pathogenicity per se. These fungi may nevertheless be involved in the production of certain tastes and odours in water. Growth requirements Acremonium requires very wet conditions, e.g. building materials with high water affinity. Consequently it is often seen growing in combination with *Stachybotrys*, a tertiary coloniser. Most species do not grow at 37°C {813}. Water Activity : Aw: 0.90-0.98 Growth on building materials or indoor environment Acremonium grows well indoors under very wet conditions {813}. When found indoors, it usually originates either from outdoor air or from contaminated crawl spaces {2104} or from contaminated building materials following an incidence of water damage. However, the spores of this fungus are formed in a slimy mass resulting in limited aerosolisation: therefore its prevalence may be low in air samples {1973}. Acremonium has been found indoors growing on building materials, such as acoustic and thermal fibreglass insulation used in heating ventilation and air conditioning systems. Because of its high water affinity, it is often isolated from cooling coils, drain pans, window seals and water from humidifiers. More details Acremonium has often been reported associated with contamination by *Stachybotrys chartarum*, as this fungus is also favoured by very wet circumstances. A stench in the air may be associated with the presence of this fungus {431}. In indoor investigations, Acremonium occupied a middle to low rank among the dominant genera in winter and summer in Argentina {1584}. The same can be said of homes in Southern California, where Acremonium was not among those most frequently isolated, although it was found in 35% of homes tested, with a mean viable spore concentration of 30.6 CFU/m³ {1824}. Conversely, a one year survey of outdoor air of a Brazilian city showed a low prevalence of Acremonium (0.2%), ranking 19th rank among the 25 genera identified {1973}. In an investigation of the presence of indoor air fungi in eight houses in Finland, Airaksinen et al {2104} found Acremonium in a majority of dwellings with a mean concentration of 160 CFU/m³. Moreover, higher concentrations were identified in crawl spaces (mean concentration 2 240 CFU/m³) hence enabling the authors to establish a clear link between fungal spores in the indoor air and contaminated crawl space. In another study, among 53 species, Acremonium strictum was found in 25% of air samples (but not in water) of water closet environments and thereby considered as one of the most prevalent species {2193} in this study. Patovirta et al. {199} performed a follow-up study after an extensive mould remediation in school buildings; Acremonium sp. was found in the air and on building materials prior to and shortly after remediation but not after an extended period of 3 years. Elsewhere, Acremonium was identified in 14 out of 72 samples of materials from 23 mould-infested buildings and was ranked 7th among the most frequent genera isolated {725; 605}. As with other fungi, Acremonium was most often found on wood {605}. Acremonium strictum and Acremonium sp. were also found in carpet dust samples in Belgian homes, at concentrations of 104 CFU/g of dust {3972}. In a controlled study on mould growth on wet gypsum wallboard in an indoor environment, Acremonium was among early colonisers, along with *Cladosporium* and *Penicillium*; it was detected three weeks after immersing the building material in water {4080; 587}. Normal laboratory precautions should be exercised in handling cultures of this species within Biosafety Level 2 practices and containment facilities. Acremonium grows well on general fungal media, maturing within 5 days. Colonies may be slow to moderately rapid when grown at 25 °C; colonies are often compact, reaching less than 2.5 cm in diameter in 5-10 days {3283; 1056; 413}. Colony texture is at first glabrous, compact, sometimes moist, flat or folded, then subseqly felt-like and, with age, becomes overgrown with loose hyphae: at this stage, the colonies appear powdery in texture, suede-like or floccose. Colonies may be white, pale grey, pink, rose or orange in color {814; 813; 412; 1056}. The reverse side is either uncoloured or tinted by a pink to rose coloured pigment {4080; 3283; 415}. Microscopic morphology The Acremonium septate hyphae are hyaline and very delicate. Vegetative hyphae often form hyphal ropes. The conidiogenous cells are phialides. The phialides are solitary, aculeate, mostly awl-shaped, simple, erect, and arise from the substrate mycelium or from bundled aerial hyphae (fasciculate). The unbranched phialides are separated from the hyphae by a septum and taper towards their apices. When conidiophores occur, their branches are only restricted to the basal part. Conidia are oblong (1.3 x 4-8 mm), usually one-celled, hyaline or pigmented. They usually appear in clusters, in balls or rarely as fragile chains; the conidia may be aggregated in slimy heads at the apex of each phialide, bound by a gelatinous material {814; 812; 1056}. More details The conidia are mainly single-celled or rarely multicellular (2- or 3-celled conidia), fusiform with a slight curve or may resemble a shallow crescent. These structural properties of conidia vary depending on the species; for example, Acremonium falciforme usually produces crescent-shaped, nonseptate conidia. Acremonium spp., as most fungi, produce various hydrocarbons, alcohols, ketones, esters and terpenes, in nature as well as on building materials {594; 2076}. Production of microbial volatile organic compounds (MVOCs) is influenced by both medium and species. One study was able to detect cyclotrisiloxane, limonene, pentane, arsenous acid and benzene on fibreglass experimentally colonised with Acremonium {2051}. More details A number of organic compounds, including volatile organic compounds (VOCs), have been identified in indoor air in damp buildings contaminated by fungi; these VOCs are thought to contribute to various indoor air problems. However, most of the identified metabolites are non-reactive and found in low concentration in indoor air {594}. Some species have a defined MVOC profile that may be subject to considerable modification in response to external factors such as cultivation on different substrata. These differing substrata change both the number and concentration of MVOCs {2968; 2809; 1148} whereas other volatile metabolites are specific for single species {2809}. Mycotoxins Some species of Acremonium produce mycotoxins. Among the best studied mycotoxins produced by Acremonium spp. are citrinin, cephalosporin, ergovaline {2109} and lolitrem A and B. For instance, lolitrem produced by Acremonium lolii are potent tremorgens found in contaminated grasses {4305; 2192}. Acremonium species can produce potent trichothecene mycotoxins under certain conditions {431}; to date, this toxin production has been associated solely with substrates of contaminated food, fodder and pasture. Most Acremonium toxins are associated with rural settings. More details A novel mycotoxin named acrebol, consisting of two closely similar peptaibols, was isolated from an indoor strain of Acremonium exuviarum {4336}. Acrebol induces necrosis-like cellular death in mouse insulinoma MIN-6 cells. Acremonium conocephalum can produce alkaloids that are responsible for fescue toxicity {4321} ; it is not clear whether the toxic principle is produced directly by the fungus alone or whether it is the product of a symbiotic fungus-plant association. The resulting mycotoxins is known as summer fescue toxicosis {4305} (see Mycotoxins section). A novel Acremonium metabolite, named FR235222, possesses potent immunosuppressive properties on mouse cell lines. The potential clinical use of this molecule is currently under study {2111}.

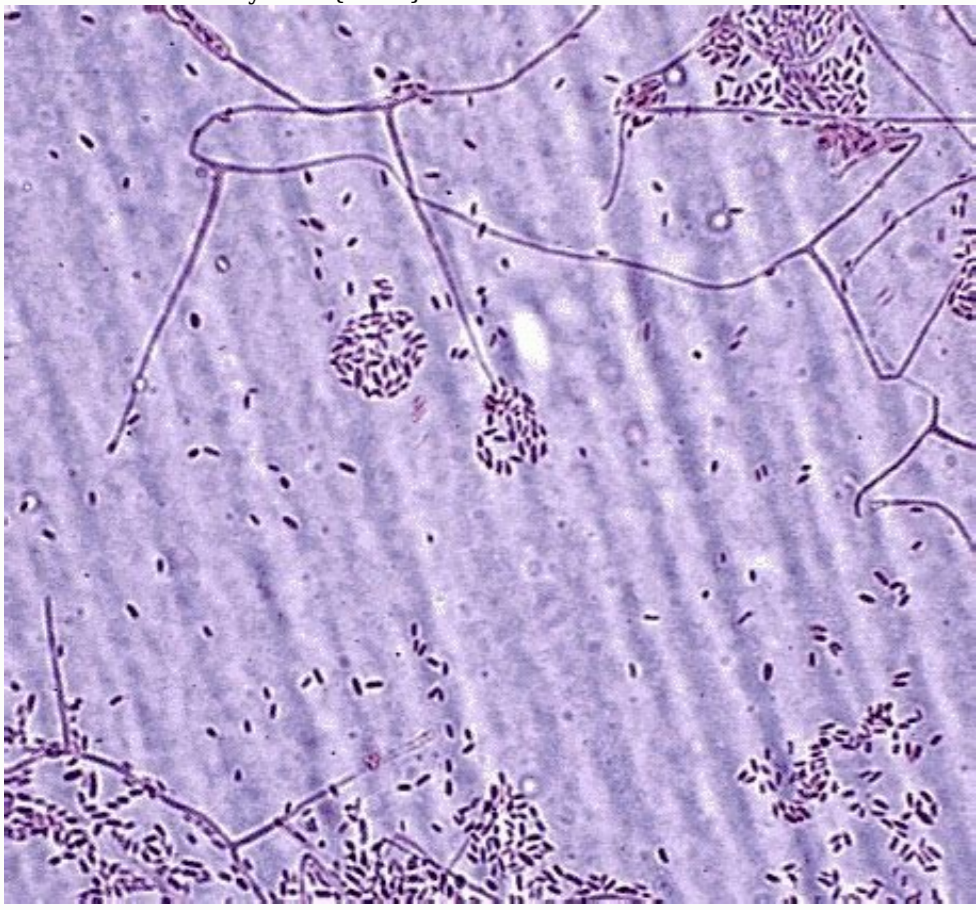


No specific irritation or inflammation symptoms have been attributed specifically to Acremonium spp. Many substances common to most moulds, such as glucans, may cause irritation and inflammation in the exposed subject. However, no particular substance has been reported in relation to Acremonium. More details Generally speaking, all moulds contain substances that are irritants and promote inflammation to some degree. Some VOCs produced by moulds in the indoor setting on damp building materials are thought to contribute to various health problems such as eye irritation, irritation of the nose and throat, lethargy and headache {594} (1-→3)-Beta-D-glucans are non-specific and non-allergenic structural cell wall components present in most fungi and have been suggested to play a causal role in the development of respiratory symptoms associated with indoor fungal exposure {1346}. Allergic reactions Some species of Acremonium have been reported to be allergenic and have been linked to Type I allergies (hay fever and asthma) {3286; 2342; 3095; 388}. However the few aerobiological surveys that have detected Acremonium indoors report a low prevalence from 4.6% {4321} to slightly above 10% {4274}; this fungus rarely appears in large quantities. Consequently, the contribution of Acremonium to fungal allergies is likely low. Allergic components and mechanism No specific allergenic fraction of Acremonium is listed with either the Biological Product registry of the Federal Drug Administration (FDA) {3285} or with the International Union of Immunological Societies. Hypersensitivity pneumonitis Type III hypersensitivity pneumonitis due to Acremonium sp. has been reported in a few instances, mostly associated with contaminated home humidifiers {2761; 4322; 1407}.

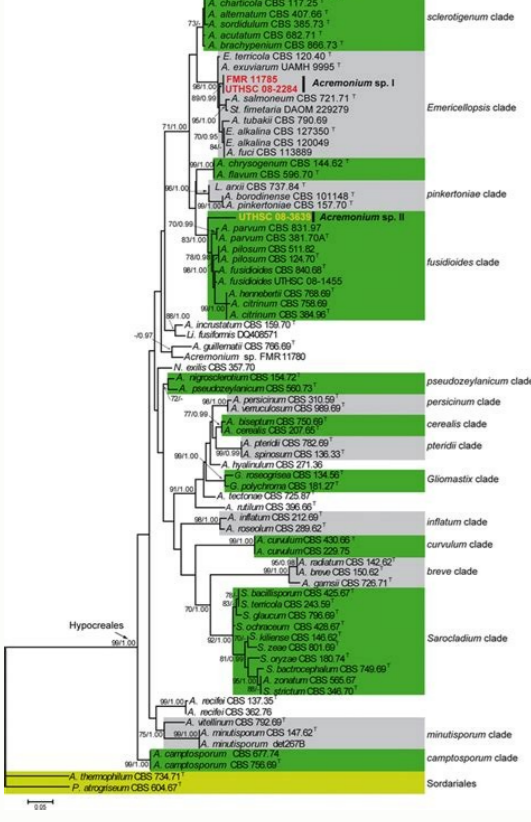


In one study, hypersensitivity pneumonitis associated with contaminated home ultrasonic humidifiers was diagnosed in five patients. Tests for precipitating antibodies against an extract of the humidifier water yielded strong positive reactions in all patients tested; all patients also tested positive for precipitins against *Cephalosporium acremonium* (syn. *Acremonium chrysogenum*) {1407}. Two other cases of hypersensitivity lung disease apparently caused by home environment contamination by *Cephalosporium* have been identified {4322}; one case was presumptively in a home contaminated by sewage flooding and the other as a result of exposure to humidifier contaminated water. Toxic effects (mycotoxicosis) Many strains of Acremonium are active producers of toxins under given sets of growth conditions. Toxic effects due to ingested Acremonium toxins include cytotoxic, nephrotoxic and tremorgenic effects. These pathologies are well known to occur in livestock and other animals {3182; 3184; 3185; 4305} but no cases of human mycotoxicosis have yet been reported. Animal cases of neurotoxic mycotoxicosis have often been reported associated with Acremonium contamination of grasses and feed {2192}. In particular, Acremonium infected tall fescue grasses may be responsible for toxicosis reported in both sheep and cattle, including Staggers disease as well as failure to thrive in cattle {4327}. More details Clinical signs of Staggers disease are transient ataxia, which is aggravated by stimulation; nearly complete recovery occurs after removal of ryegrass as the primary forage. Morbidity associated with these toxicoses is high {4324}. Acremonium conocephalum, an endophytic fungus commonly found in tall fescue, has been identified as the cause of poor performance of beef cattle and horses fed on tall fescue. Summer fescue toxicosis or fescue poisoning is a disease caused by ingestion of Acremonium contaminated tall fescue grass; it produces a dry gangrenous lesion in affected livestock (rarely sheep) similar to that found in ergot poisoning {4305; 2189}. For many years, endophytic mycotoxin intoxications have been limited to the United States and New Zealand. However, these mycotoxicoses have since been reported in Western Europe {4324}.

Experimentally, injections of ryegrass extracts containing the tremorgenic mycotoxin lolitrem-B into mice induce signs of toxicosis {2185; 4326; 2192; 4327}. Infections and colonisations Acremonium species are infrequent pathogens in humans {2152; 2131}. However, they can cause a spectrum of infections, ranging from mycotic keratitis and mycetoma in the normal host, to fungemia, disseminated infections and cutaneous infections in immunocompromised subjects {2105; 316}. Opportunistic infections leading to respiratory infections, infections of the cornea and nails {2134} in individuals with weak immune systems have been occasionally reported. Life-threatening unusual pulmonary mycoses caused by *A. strictum* have been reported in patients with haematological diseases {2139}. Acremonium mycetomas and other rare hyalohyphomycoses infections have been reported in immunodeficient patients and in immunocompetent subjects with wound injuries. This fungus has also been involved as the aetiological agent of a few cases of vertebral osteomyelitis {2085}.



About 10 species of Acremonium are reported as causes of infection in vertebrates, with *A. kilianse* being the most important {2085}. Agents of Acremonium hyalohyphomycoses include, in alphabetical order, *A. alabamensis*, *A. falciforme*, *A. kilianse*, *A. potroni*, *A. ricei*, *A. roseo-griseum* and *A. strictum* {2121; 2092; 2091}. However, many case reports of infections only identify Acremonium species at the genus level. Clinical manifestations of these hyalohyphomycoses caused by Acremonium include arthritis, osteomyelitis, peritonitis, endocarditis, pneumonia, cerebritis and subcutaneous infection {814}. This pathogen has also been reported to cause locally invasive diseases such as mycetoma, paranasal sinus and haemodialysis access graft infections as well as posttraumatic keratitis {2199}. More details Acremonium is usually of low pathogenicity {2102}, although this fungus is becoming increasingly recognised as an opportunistic pathogen causing a variety of infections in immunocompromised patients (organ transplant recipients, myeloma or leukemia patients and those receiving corticoid therapy) {2167; 2085; 2126}. Invasive or disseminated infections are almost exclusively observed in immunocompromised patients {2114; 2089}; among neutropenic patients suffering from a disseminated infection, about half of afflicted patients died {2159}. The lungs and the gastrointestinal tract are the apparent portals of entry in many patients {316}, although the spectrum of invasive disease is large, ranging from sinusitis, osteomyelitis, arthritis, peritonitis and pneumonia; invasion of vascular structures results in thrombomycosis, tissue infarction and necrosis {2114}. In immunocompetent individuals, it is possible to contract an Acremonium infection due to traumatic penetration of the mould {2102}; high prevalence of Acremonium species in soil can lead to superficial infections after traumatic inoculation {2159}. In these cases, the clinical portrait is most commonly foot mycetomas or corneal infections following penetrating injuries {2081; 2091} or contamination of organ-cultured cornea {2097}. Keratomycosis may also develop in individuals who wear contact lenses {2114} or following a prior keratitis infection {2131}. Fungal keratitis has also been reported following infectious endophthalmitis {2153}. Ocular infections represent the second most common Acremonium disease {2105}. Acremonium mycetoma occurs only in certain tropical or sub-tropical countries; it is a chronic infection of the distal extremities usually causing only mild discomfort, although a prolonged infection can lead to underlying bone destruction. Virulence factors No particular virulence factor has been reported and most species of Acremonium do not grow at 37°C. Acremonium sp. infections have occasionally been reported in the hospital setting {3257; 2199; 2167; 2197; 4229}. However, true nosocomial transmission of Acremonium spp. has rarely been reported. Notwithstanding this nominal occurrence, Acremonium species have become significant problems in the treatment of immunocompromised hosts, causing life threatening invasive infections: fungi of this genera are to be considered, for the time being at least, as emerging pathogens if not future nosocomial threats {366; 2172; 2123}. Acremonium spp. have nonetheless been very seldom reported in true nosocomial infections. Molecular studies have not been reported, but environmental and clinical isolates have been compared for phenotypic and biochemical similarities. In an American study, Acremonium has been identified in hospital ventilation systems {2174}. Eleven air filters from seven hospitals in the Eastern United States were selected on the basis of deposits on the filter media; Acremonium obclavarum was a cultured species in the air filters of only one hospital, indicating it was not a major fungal contaminant, as opposed to other moulds such as *Aspergillus*, *Cladosporium* or *Alternaria* {386}. Iatrogenic Acremonium infections have not been well studied; however, Acremonium sp. has been associated with a confirmed case of mechanical valve endocarditis {2099} and with a case of fungal peritonitis in a patient undergoing peritoneal dialysis {2116}. Furthermore, extrinsic contamination of multidose vials of an injectable radioactive solution for nuclear medicine procedures has been reported, although this was not associated with any clinical disease {4328}. Moreover, Acremonium sp. was isolated from surgical instruments, including an endoscope, due to contamination by rinse water used in the reprocessing of the device {2124}. More details There have been reports of disseminated Acremonium infections in mild or severely immunocompromised individuals.



The mechanism of disseminated infection is thought to be secondary to increased host susceptibility with prior colonisation. A recent outbreak of *Acremonium kilense* endophthalmitis was reported following cataract surgery in an ambulatory surgical center in which the responsible reservoir was determined to be a contaminated humidifier within the heating, ventilation, and air-conditioning system located directly above the operating suite [2174]. This occurrence was somewhat surprising since, historically, only *Aspergillus* spp.



and Zygomycetes have been implicated as major airborne fungal pathogens occurring in immunocompromised patients in health care settings, usually associated with hospital construction or renovation [4330]. Many cases of post transplantation *Acremonium* infections underscore the nosocomial threat posed by this fungus even if hospital transmission is not incriminated. Indeed, *Acremonium* has been involved in infections following transplantation of blood stem cells [2089], bone marrow [2091] or kidney [2112; 2139]. Fatal infections by *A. strictum* have also been reported in young patients with leukemia [2092; 2171; 2126]. A case an acute septic arthritis after kidney transplantation due to *Acremonium* species was also reported [2112].

Finally, very rare cases of neonates with disseminated *Acremonium* infection have been recorded [2108]. Occupational diseases No occupational infections due to *Acremonium* sp. have been reported associated with specific occupations. No particular outbreaks due to exposure to *Acremonium* sp. have been reported in the workplace. More details Type III hypersensitivity pneumonitis due to *Acremonium* spp. have been mostly reported in the home environment and is not particularly known in occupational settings. Because of the prevalence of *Acremonium* in both cold and warm weather pastures, occupational exposure can theoretically be a risk in the rural setting. The same may be said of *Acremonium* allergy as this fungus has been reported to be present in farm buildings and that these airborne fungal spores may be transported from cow barns to farmers' homes [2203]. It is worthwhile mentioning that *Acremonium* species are ubiquitous and often considered laboratory contaminants. However, because the clinical presentation of an *Acremonium* mycetoma is not distinctive [2155] and because *Acremonium* hyalohyphomycoses are very seldom considered when conducting primary cultures of deep sited specimens, it is important to verify the possibility of this aetiology in the presence of positive cultures. Histopathology The histological presentation of a deep sited infection due to *Acremonium* is typically that of an opportunistic fungal hyphal infection; for example, *Fusarium* and *Acremonium* species cannot be distinguished by histopathological examination alone [2092]. Pathologists may make a preliminary identification of this fungus in cases of invasive hyalohyphomycoses [2156] and keratitis by observing a combination of histological features, including hyaline septate hyphae and characteristic reproductive structures known as phialides and phialoconidia in tissue sections routinely stained with haematoxylin and eosin, Gomori methanamine silver and/or periodic acid-Schiff stains; cultures are required to complete the diagnosis [2156]. In one instance, *A. strictum* was shown to cause a dense nodular lymphohistiocystis infiltrate cutaneous infection [2156]. *Acremonium* mycetomas produce pale grain eumycetoma with an inflammatory response and grain morphology that are very similar to those caused by other organisms. *Fusarium* and *Acremonium* grains usually have a minimal fringe and contain a dense mass of intermeshing hyphae. However the features separating *Pseudallescheria boydii*, *Fusarium* and *Acremonium* grains are not invariable and can only be used as an approximate guide in correctly identifying the organism [4322]. Immunodiagnosis *Acremonium kilense* (syn., *Cephalosporium acremonium*) allergens are available and still recommended for routine IgE testing and skin testing. Immunodiagnostic reagents for *Acremonium* sensitisation (skin testing) are often still listed under *Cephalosporium* sp. and may hence cause some confusion [4334; 3284; 3730]. In one study, the frequency of *Acremonium* sensitivity was 16% in a group of 101 patients with allergic bronchial asthma [4335]. Precipitating antibodies to *Acremonium* have been found in patients with allergic alveolitis and hypersensitivity pneumonitis [4322; 4333; 1407]. More details The only common commercially available allergen preparations for use in vivo and/or in vitro are listed under *Cephalosporium acremonium* [3284; 3730]; no commercial reagent has been established for IgG or precipitin testing. The *Acremonium* allergen extract listed by the FDA is as follows: GJ30 - *Cephalosporium acremonium* {3285}. Test IgE IgG Antigens Other Skin Tests X RAST-IgE X RAST-IgG Experimental ELISA-ELIFA Immunodiffusion Experimental Immunofluorescence Complement fixation PCR Other 199. Patovirta, R. L., Reiman, M., Husman, T., Haverinen, U., Toivola, M., and Nevalainen, A. (2003). Mould specific IgG antibodies connected with sinusitis in teachers of mould damaged school: a two-year follow-up study. *Int J Occup. Med Environ Health*. 16[3], 221-230. 366. Groll, A. H. and Walsh, T. J. (2001). Uncommon opportunistic fungi: new nosocomial threats. *Clin Microbiol Infect*. 7 Suppl 2:8-24. 8-24. 386. Simmons, R. B., Price, D. L., Noble, J. A., Crow, S. A., and Ahearn, D. G. (1997). Fungal colonization of air filters from hospitals. *Am Ind Hyg Assoc J*. 58[12], 900-904. 412. Larone, D. H. (1987). *Medically important fungi: A guide to identification*. 2nd edition. 230 p. New York - Amsterdam - London, Elsevier Science Publishing Co., Inc. 415. St-Germain, G. and Summerbell, R. (1996). *Champignons filamenteux d'intérêt médical. Caractéristiques et identification*. 314 p. Belmont, Star Publishing Company. 431. Roberts, S. (2006). Mold...What is all about? p. 1-p. 7. *Mold-Help*. 3-10-0060.

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