Opportunistic mycosis: Penicillosis

Penicillium: - is a genus of ascomycetous fungi of major importance in the natural environment as well as food and drug production.

Some members of the genus produce penicillin, a molecule that is used as an antibiotic, which kills or stops the growth of certain kinds of bacteria inside the body. Other species are used in cheese making. According to the Dictionary of the Fungi (10th edition, 2008), the widespread genus contains over 300 species.

Species:

* *Penicillium marneffei*, a thermally dimorphic species endemic in South East Asia, which presents a threat of systemic infection to AIDS patients.

* *Penicillium camemberti*, which is used in the production of Camembert and Brie cheeses.

* *Penicillium candidum*, which is used in making Brie and Camembert. It has been reduced to synonymy with *Penicillium camemberti*

* *Penicillium chrysogenum*, which produces the antibiotic penicillin

* *Penicillium roqueforti*, which is used in making Roquefort, Danish Blue cheese, and also recently Gorgonzola

* *Penicillium verrucosum* produces ochratoxin A

* *Penicillium viridicatum* produces ochratoxin

Characteristics:

The thallus (mycelium) typically consists of a highly branched network of multinucleate, septate, usually colorless hyphae. Many-branched conidiophores sprout on the mycelia, bearing individually constricted conidiospores. The conidiospores are the main dispersal route of the fungi, and often are green in color.

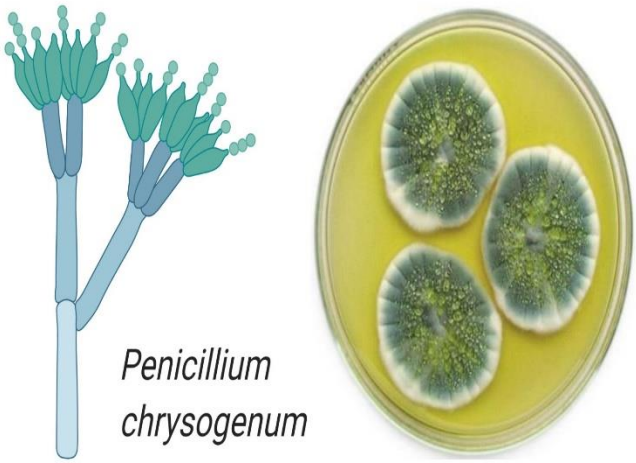
Sexual reproduction involves the production of ascospores, commencing with the fusion of an archegonium and an antheridium, with sharing of nuclei. The irregularly distributed asci contain eight unicellular ascospores each.

Economic value

Several species of the genus Penicillium play a central role in the production of cheese and of various meat products. To be specific, Penicillium molds are found in Blue cheese. *Penicillium camemberti* and *Penicillium roqueforti* are the molds on Camembert, Brie, Roquefort, and many other cheeses. *Penicillium nalgiovense* is used to improve the taste of sausages and hams, and to prevent colonization by other molds and bacteria

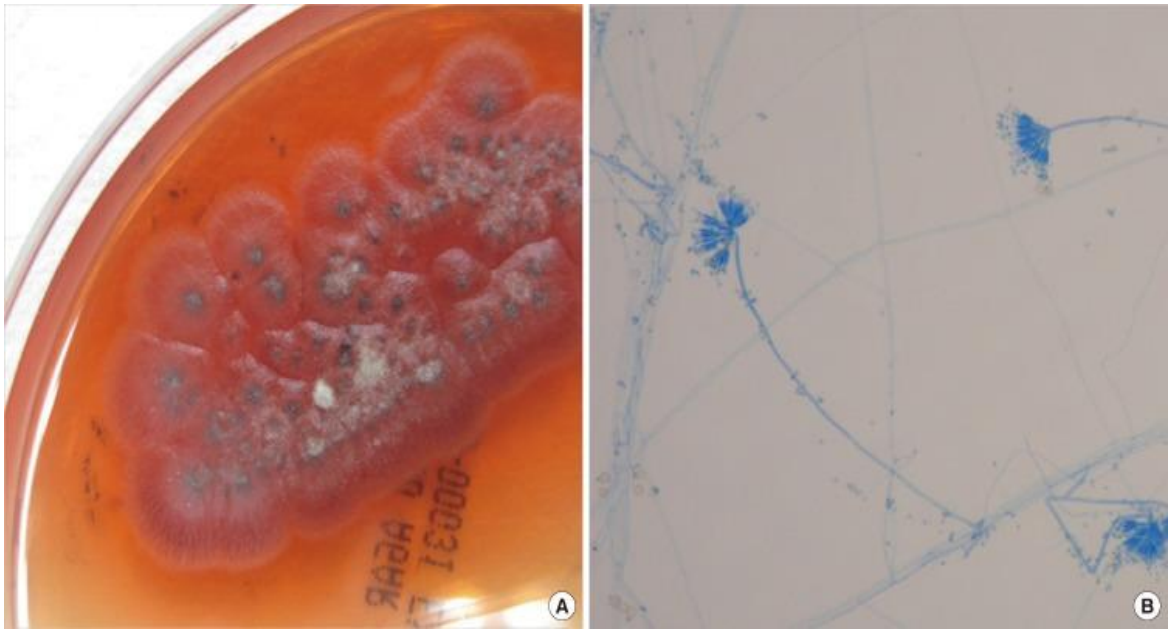
In addition to their importance in the food industry, species of *Penicillium* and *Aspergillus* serve in the production of a number of biotechnologically produced enzymes and other macromolecules, such as gluconic, citric, and tartaric acids, as well as several pectinases, lipase, amylases, cellulases, and proteases. Some Penicillium species have shown potential for use in bioremediation because of their ability to break down a variety of xenobiotic compounds.

The genus includes a wide variety of species molds that are the source molds of major antibiotics. Penicillin, a drug produced by *P. chrysogenum* (formerly *P. notatum*), was accidentally discovered by Alexander Fleming in 1929, and found to inhibit the growth of Gram-positive bacteria.



Penicillium marneffei

Penicillium species are usually regarded as unimportant in terms of causing human disease. *Penicillium marneffei*, discovered in 1956, is different. This is the only known thermally dimorphic species of *Penicillium*, and it can cause a lethal systemic infection (penicilliosis) with fever and anemia similar to disseminated cryptococcosis.



Epidemiology

There is a high incidence of penicilliosis in AIDS patients in SE Asia; 10% of patients in Hong Kong get penicillosis as an AIDS-related illness, Cases of *P. marneffei* human infections (penicillosis) have also been reported in HIV-positive patients in Australia, Europe, Japan, the UK and the U.S.. All the patients, except one, had visited Southeast Asia previously

Discovered in bamboo rats (Rhizomys) in Vietnam, it is associated with these rats and the tropical Southeast Asia area. *Penicillium marneffei* is endemic in Burma (Myanmar), Cambodia, Southern China, Indonesia, Laos, Malaysia, Thailand and Vietnam.

Although both the immunocompetent and the immunocompromised can be infected, it is extremely rare to find systemic infections in HIV-negative patients.

The incidence of *P. marneffei* is increasing as HIV spreads throughout Asia. An increase in global travel and migration means it will be of increased importance as an infection in AIDS sufferers

Penicillium marneffei has been found in bamboo rat faces, liver, lungs and spleen. It has been suggested that these animals are a reservoir for the fungus. It is not clear whether the rats are affected by *P. marneffei* or are merely asymptomatic. carriers of the disease.

Clinical Presentation:

Patients commonly present with symptoms and signs of infection of the reticuloendothelial system, including generalized lymphadenopathy, hepatomegaly, and splenomegaly. The respiratory system is commonly involved as well; cough,

fever, dyspnea, and chest pain may be present, reflecting the probable inhalational route of acquisition. Approximately one-third of patients may also exhibit gastrointestinal symptoms, such as diarrhea.

Laboratory diagnosis

The fact that *Penicillium marneffei* is thermally dimorphic is a relevant clue when trying to identify it. However, it should be kept in mind that other human- pathogenic fungi are thermally dimorphic as well. Cultures should be done from bone marrow, skin, blood and sputum sample

Plating samples out onto two Sabouraud agar plates, then incubating one at 30 °C and the other at 37 °C, should result in two different morphologies. A mold-form will grow at 30 °C, and a yeast-form at 37 °C

Mycelial colonies will be visible on the 30 °C plate after two days. Growth is initially fluffy and white and eventually turns green and granular after sporulation has occurred. A soluble red pigment is produced, which diffuses into the agar, causing the reverse side of the plate to appear red or pink. The periphery of the mold may appear orange-colored, and radial sulcate folds will develop.

Under the microscope, the mold phase will look like a typical *Penicillium*, with hyaline, septate and branched hyphae; the conidiophores are located both laterally and terminally. Each conidiophore gives rise to three to five phialides, where chains of lemon-shaped conidia are formed On the 37 °C plate, the colonies grow as yeasts. These colonies can be cerebriform, convoluted, or smooth. There is a decreased production in pigment, the colonies appearing cream/light-tan/light-pink in color. Microscopically, sausage-shaped cells are mixed with hyphae-like structures. As the culture ages, segments begin to form. The cells divide by binary fission, rather than budding. The cells are not yeast cells, but rather arthroconidia. Culturing isn't the

only method of diagnosis. A skin scraping can be prepared, and stained with Wright's stain. Many intracellular and extracellular yeast cells with cross walls are suggestive of *P. marneffei* infection. Smears from bone marrow aspirates may also be taken; this is regarded as the most sensitive method.

These samples can be stained with the Giemsa stain. Histological examination can also be done on skin, bone marrow or lymph nodes.

The patient's history also is a diagnostic help. If they have traveled to South east Asia and are HIV-positive, then there is an increased risk of them having penicilliosis.

Antigen testing of urine and serum, and PCR amplification of specific nucleotide sequences have been tried, with high sensitivity and specificity.

Rapid identification of penicilliosis is sought, as prompt treatment is critical.

Treatment should be provided as soon as penicilliosis is suspected.

Treatment:

Two weeks of amphotericin B, then 10 weeks of oral itraconazole.

Genomics Sexual reproduction

P. marneffei had been assumed to reproduce exclusively by asexual means based on the highly clonal population structure of this species. However, studies by Henk et al. (2012) revealed that the genes required for meiosis are present in *P. marneffei*. In addition, they obtained evidence for mating and genetic recombination in this species. Henk et al. concluded that *P. marneffei* is sexually reproducing, but recombination in natural populations is most likely to occur across spatially and genetically limited distances resulting in a highly clonal population structure. It

appears that sex can be maintained in this species even though very little genetic variability is produced.