Fungal Disease and Therapy

**Corresponding Author:**
Dr. Gam L Harn,
Lecturer, USM - Malaysia

**Submitting Author:**
Mr. Chai C Hean,
student, USM - Malaysia

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Author(s): Hean C C, Abdul Rahim I B, Harn G L, Ahmad Halimi N B, Hamzah M B, Fatimah Aisyah T , Said N B

Abstract

There are many types of fungal disease include superficial mycoses, cutaneous mycoses, subcutaneous mycoses, systemic mycoses, opportunistic mycoses and non-opportunistic mycoses. Onychomycosis is one type of superficial mycoses which normally occurs in finger and toe nails. It is diagnosed by using direct microscopy and culture to identify whether the causing agents are dermatophytes, yeast or molds. Terbinafine is the normal drug used to treat onychomycosis given by oral or cream form. Histoplasmosis is a systemic infection which infects the lungs first then spread to other parts the body. For its diagnosis, several methods chest X-ray, computerized tomography (CT) scan, fungal culture and blood test are used to identify the causing agent which is H.capsulatum. Aspergillosis is a type of opportunistic fungal infection which spread throughout the body usually caused by Aspergillus fumigatus and Aspergillus niger. It is difficult to diagnose aspergillosis as it normally infects immunocompromised patients and biopsies are one of the ways to diagnose aspergillosis in healthy patient. Itraconazole is the common drug to cure aspergillosis and histoplasmosis.

Introduction

Fungi are a group of non-photosynthetic microorganisms which normally found in soil or dead organic matter. It can also act as parasites in animals or humans. Fungi can survive in almost anywhere despite of the extreme conditions of the surroundings such as very low temperate and high pressure. Fungi usually spread by spores which can be blown to a distance of 500km and enter animal or human respiratory tract and open wound for infection. Fungi which also known as mycoses can be classified into 3 classes namely eukaryotes, yeast and moulds. Most fungi are in microscopic multi-cellular filaments and some are macroscopic in size such as mushroom. (Josephine, 2011) The invasion of these fungi into human body can lead to fungal infection. There are several types of fungal infection which are superficial mycoses, cutaneous mycoses, subcutaneous mycoses, systemic mycoses, opportunistic mycoses and non-opportunistic mycoses. All the mycoses infect human body at distinct location and lead to deterioration of human health. In this report, onychomycosis, aspergillosis, histoplasmosis are the main topics and explained in detail. The superficial mycoses are usually occurring at the outer layer of the skin, hair, and nails. Tissue and organs in the body are rarely infected. Superficial mycoses can be classified into many classes namely dermatophytosis, candidiases and malassezia infection. (Vieira, 2011)

Onychomycosis is a fungal infection that affects the toenails or the fingernails. (Boni, 2010) It is under superficial dermatophytosis fungal infection. The term onychomycosis is divided into 2 parts, onycho- refers to nails and –mycosis refers to a fungal infection. (John Ratz, 2011) This fungal infection usually occurs in adult men with a percentage about 54-70%. Dermatophytes, yeast, and nondermatophyte molds are the three main fungi which cause onychomycosis. (Arenas, 2001) The dermatophytes is the main class of fungi that cause this onychomycosis infection. Trichophyton rubrum and Tricophyton mentagrophytes have a record 90% of the all onychomycosis cases, which they both cover 70% and 20% out of total 90% cases respectively. (Boni, 2010) On the other hand, candida species such as Candida Albican can contribute to the onychomycosis infection. A report from Singapore stated that Candida species are commonly isolated from the nails infection especially for females. (Hiok-Hee, 2005) Meanwhile, non-dermatophytes are becoming the more popular causing agents and it covers up to 15% from the total onychomycosis cases in certain country. (Boni, 2010) Infection starts on the lateral borders of the nails is known as the distal and lateral subungual onychomycosis. In this type of onychomycosis, there is no early sign and symptoms, the symptoms established after infection are nail thickening, fragility, striae and a yellow discoloration of the nails. This infection can cause the pain, discomfort or even serious occupational and physical limitation. Besides, people often experiences emotional problem which affects the quality of their life. (Boni, 2010) Geriatric patients are the most popular group for being infected by onychomycosis. Toenails are more often infected compared to fingernails and onychomycosis rarely occurs in children. (Romano, 2005) There are some factors which increases the opportunity of onychomycosis infection such as male sex, genetic susceptibility, smoking, environmental and behavioural
Histoplasmosis is a fungal infection caused by the fungus named Histoplasma Capsulatum. It is endemic and spread worldwide including United States where most cases are reported from Missississipi and Ohio River Valley regions. (Kauffman, 2006) H.capsulatum is a fungus that lives in the nitrogen-rich soil and also soil with birds and bat droppings. Fungi are usually found in the bats’ dropping but not the birds’ dropping. Soil is contaminated with H.capsulatum which is in mycelia form. Then, the fungi are introduced into the air. When people constantly inhale the air, the spores enter the alveolar space of the lung and invade the body. At body temperature (36.9ºC), the fungi germinate into yeast form, multiply and move to other parts of body.

Most of the healthy people do not develop any symptoms. The types of histoplasmosis depend on the symptoms shown by the patients. The first one is asymptomatic pulmonary histoplasmosis in which people do not show any symptoms of infection. (All about Pharmacy and Drugs, 2006) This is type of infection usually ignored by patients and no treatments are given. Several ways diagnose the infection is by X-ray and imaging. However, this could not be a deduction that the person might have fungi infection and detailed diagnosis need to be carried out. Next, patients with acute symptomatic pulmonary histoplasmosis have a flu-like symptom that ranges from mild to severe flu. Fever, colds, cough, chest pains, lost of weight, erythema nodosum and headache are some of the symptoms when a patient inhaled a high concentration of H.capsulatum spores. Disseminated histoplasmosis occurs when immunocompromised patients who have AIDS, undergone organ transplant, chemotherapy and corticosteroid therapy inhale a high amount of H.capsulatum spore into the lung. Besides, children are more susceptible disseminated histoplasmosis infection. This infection can invade to other organs such as liver, heart, brain and gastrointestinal tract. Symptoms are chills, fever, short of breath, hypotension and sepsis. They might also have night sweat, fatigue, enlarged liver and spleen for months. Some patients also experienced ulceration in mouth. Chronic pulmonary histoplasmosis occurs in patients having lung disease such as emphysema. Fever, fatigue, cough with sputum and weight loss are some of the common symptoms.

Aspergillosis is common in the community (Virtualmedicalcentre, 2005). According to Pubmed/Medline literature search, Malaysia was included in the developing countries list that had a reported case series of Aspergillosis but the exact disease frequencies are unknown. This infection was a vital reason for morbidity and mortality of hospitalized patients in developing countries (Chakrabarti, Chatterjee, Das, and Shivaprakash, 2011).

Aspergillosis is an infection caused by the fungus Aspergillus which is a mould that spreads through the air and found in organic matter. There are more than 100 Aspergillus species but Aspergillus fumigatus and Aspergillus niger are the common causing agents and less likely caused by Aspergillus flavus and Aspergillus clavatus. (Gabino J, 2004). Aspergillus’ spores are present in the air we breathe, but it is not harmful to normal and healthy people. (The Aspergillus Website, 2011) This is due to persons with good immune system who inhale spores of Aspergillus usually develop an acute diffusive pneumonia but it will be self-recover. (Aspergillosis, 2011) However for those immunocompromised patients such as those who have congenital immunodeficiency disorders or HIV, they may be susceptible to Aspergillus infection. (Joel E. Gallant & Andrew H. K.1996) Thus, it is considered as an opportunistic fungal infection.

Aspergillosis involves both infection and growth of fungus as well as allergic responses. Fungi enter human body through inhalation of air with dust and that’s the main reason why the common site of infections is the respiratory system such as lungs and sinuses. It can cause a wide range of diseases to human, ranging from hypersensitivity reactions to direct angioinvasion. (Medscape, 2011) There are four main syndromes of Aspergillus that is allergic bronchopulmonary aspergillosis (ABPA), chronic necrotizing pulmonary aspergillosis (CNPA), aspergilloma, and invasive aspergillosis. (Doctor Jorge Gabino, 2004). However, for immunocompromised patients, Aspergillus may spread beyond the lung, causing endophthalmitis, endocarditis, and abscesses in the myocardium, kidney, liver, spleen, soft tissue, and bone. Aspergillus is one of the well-known causes of fungal endocarditis after Candida species. (Medscape, 2011)

Allergic bronchopulmonary aspergillosis (ABPA) is a...
condition when patients have allergies to the spores of the Aspergillus moulds. It primarily affects patients with asthma, cystic fibrosis (CF) and bronchiectasis. Common symptoms are shortness of breath, coughing and wheezing. There are reports stated that the symptoms of ABPA are similar to those of asthma such as discontinuous episodes of feeling unwell, coughing and wheezing. (The Aspergillus Website, 2011) Some patients cough out brown-coloured sputum.

Chronic necrotizing pulmonary aspergillosis (CNPA) is a chronic pneumonic illness that commonly affects patients with pre-existing severe lung disease. It is usually found in patients with some degree of immunosuppresion or those who experience cystic fibrosis, bronchiectasis, inactive tuberculosis. Previous records stated that pulmonary tuberculosis patients are most susceptible to CNPA infection. (Nihon Rinsho, 2011) Besides, alcoholism and long-term corticosteroid therapy also leads to CNPA. (The Aspergillus Website, 2011) CNPA cases are uncommon and often remain unrecognized for weeks or months and this leads to a progressive cavitary pulmonary infiltrate. (Medscape, 2011)

Aspergilloma usually infects patients with pre-existing pulmonary diseases, sarcoidosis, cystic fibrosis or other lung diseases. (Hindawi.com, 2011) An aspergilloma is a fungal mass caused by a fungal infection with Aspergillus species. Aspergilloma invade either weakened lungs or pre-existing lung cavities which are usually caused by a previous infection. There are no specific symptoms but most patients cough up blood in small quantity called haemoptysis. (Medscape, 2011) This can be severe and then it requires urgent medical help.

Invasive aspergillosis is a rapidly progressive infection and often causes fatality to infected persons. Normally, it occurs in patients who are severely immunosuppresed, such as those who are profoundly neutropenic, those who have received bone marrow or solid organ transplants, and patients with advanced AIDS or chronic granulomatous disease. (Gabino J, 2004)

Diagnosis

The suitable drug of choice for treating onychomycosis is Terbinafine. Terbinafine is available both in topical (cream) and oral form. Terbinafine is mainly used in treating onychomycosis because of its antifungal activity and also because of its effectiveness to penetrate into the nail plate as proven in some previous clinical trials. (Reilly, 1996) However, the topical form is less effective in treating onychomycosis as the fungi only respond partially to the topical treatment. (Arenas, 2001) This may due to slow and partial penetration of the drug through the toenail. (Dahdah, 2006) Nevertheless, it is still used to treat the onychomycosis as the terbinafine is a potent drug.

The terbinafine tablet can be obtained in the market by the trade name of the GenRx Terbinafine or Lamisil tablet. For adult, the dose is one 250mg terbinafine tablet daily with or without foods. (Arrow – Terbinafine. 2011) Meanwhile, for children, the dose of terbinafine tablet to be taken is depending on their weight. For children weighing less than 20kg, they should consume 62.5mg daily; children with weight between 20 to 40 kg should take 125mg and more than 40kg should take 250mg of terbinafine tablet. (Arrow – Terbinafine, 2011) For the treatment of onychomycosis, the terbinafine tablet should be consumed for 6 weeks to 3 month. (GenRx Terbinafine, 2008) The duration of the time to take the tablet is depending on the instructions from the medical doctors. Besides, the duration of consuming the tablet is depending on the type and condition of the nail infection such as if the nail grow slowly or the infection is on the big toe, the duration of the consuming of the medicine might reach up to 6 month. (GenRx Terbinafine, 2008) Besides, the long term therapy with the terbinafine has a cure rate up to 90 – 100 %. (Reilly, 1996) The regime or the time for consuming the terbinafine tablet can be done by taking it at the same time each day to help the patient remember the time they consume it or depend on the direction given by the doctor. (GenRx Terbinafine, 2008) There are cases of reoccurrence of onychomycosis since the part of the nail that is infected with fungus will take a long time to grow a healthy and complete nail as the growth of the nail is relatively slow. (GenRx Terbinafine, 2008).

If the patient forgets to take the tablet, take it as soon as they remember it but if it is almost at the time taken for next dose is, the patient shall skip the missed dose and continue with next the dose. (GenRx Terbinafine, 2008) The patient should not take the dose in double even if they skip the dose as it might causes some side effects such as headache, nausea, dizziness and stomach pain. (GenRx Terbinafine, 2008). Besides, the patients also need to inform the doctors if they are pregnant or breastfeeding before taking the medicine as these conditions can cause some unwanted drug interaction with the body. For example, terbinafine can pass into the breast milk and causes side effects to the baby. (GenRx Terbinafine, 2008).

The terbinafine tablet contains of 250 mg of terbinafine hydrochloride in each tablet which is the active
ingredient of the medicine. It also contains other non-medical ingredients such as methycellulose, croscarmellose sodium, silicon dioxide and magnesium stearate. Besides, it is free from the lactose, gluten, sucrose, tartrazine or any other azo dyes. (GenRx Terbinafine, 2008).

The tablets must be kept in its pack until the time to take them and must be kept in a cool dry place (below 25°C). (Arrow – Terbinafine, 2011) It is also should be avoided from heat and dampness as it can destroy the medicine and must avoid it from the children reach. (GenRx Terbinafine, 2008).

Some common side effects of terbinafine are nausea, dyspepsia, headache and stomach pain. (GenRx Terbinafine, 2008) (Reilly, 1996) (Arrow – Terbinafine, 2011) Usually, the gastrointestinal symptoms are resulting from consuming a higher dose of tablet such as 500mg. (GenRx Terbinafine, 2008).

Both histoplasmosis and aspergillosis fungal diseases can be treated by Itraconazole. Itraconazole is one of antifungal medication effective in treating chronic pulmonary disease. It has a molecular formula C35H38Cl2N8O4 and molecular weight 705.64. (RxList, 2011) The brand name for itraconazole is Sporanox®. Itraconazole has a slower onset compared to amphotericine B. (MayoClinic.com, 2011)

It is a triazole compound and has a broad-spectrum antifungal activity such as Aspergillus species, pathogenic yeast and Histoplasmosis capsulatum. (Julie E. Mangino, Peter G. Pappas, and July 1995) This drug can be used for treating fungal infection in both HIV and non-HIV infected individuals. It can also be used as treatment for patients with fever and low white blood cell counts who are more likely infected by fungal disease. (MedicineNet.com, 2011)

For treatment of allergic bronchopulmonary Aspergillosis, Itraconazole can be chosen as a first line therapy for patients who require a reduction in corticosteroid dosage. This antifungal has clinical effects in aspergilloma, which able to act as an alternative to surgery. Itraconazole for invasive aspergillosis is often used for patients who are allergy to the Amphotericin B treatment. Itraconazole should be restricted for patients who have experience with severe toxicity of Amphotericin B therapy. (Jennings and Hardin, 1993)

The dosage form of Itraconazole is available in the form of capsules and oral solution. (Drugs.com, 2011) The usual dose of adult for Aspergillosis is 200mg to 400mg orally per day in one or two divided doses. The antifungal agent should be consumed continually for at least 3 months until clinical parameters and laboratory values indicate the infection has diminished. (Drugs.com, 2011) For Itraconazole maximal absorption, the capsules must be taken immediately after a full meal. This is because Itraconazole works well in the acidic condition. Itraconazole capsules and Itraconazole oral solution have different formulations and preparations so that they should not be used interchangeably. (RxList, 2010) However, for the serious condition, Itraconazole can be given intravenously and the recommended dose is 200 mg two times per day for four consecutive doses following by 200 mg once daily. For every infusion, the period should be more than 1 hour. (RxList, 2010)

The common side effects of Itraconazole include diarrhea, headache, nausea, vomiting, running nose and stomach ache. However, patients need to consult their doctors if they experience severe side effects such as severe allergic reactions (eg: skin rash, itchy skin), difficulty in breathing, tightness in the chest, swelling of the mouth, face, lips, or tongue, confusion, coughing up white or pink mucus, dark urine, severe stomach or back pain, unusual bruising or bleeding, vision problems (eg: blurred vision or double vision) and yellowing of the skin or eyes. (Drugs.com, 2011) Itraconazole can cause a very serious heart rhythm problem if being used with cisapride, quinidine, pimozide, dofetilide, or levacetylmethadol. (MedicineNet.com, 2011) Patients who are allergy to azole antifungal medicines, with heart failure, liver and kidney failure should take this drug with caution and this drug cannot be used in pregnant or breast feeding mother except in life threatening situation. (Sporanox capsules (itraconazole), 2011)

**Treatment**

Fungus prefers moist and dark conditions such as the nail beds of the foot. Covered shoes often do not have adequate ventilation and foot is concentrated with sweat glands which provide moisture for the fungal growth. Hence, in order to prevent from infected by onychomycosis, the cleanliness of the leg especially the nails should be taken care of. Wearing covered shoes with long hours should be prevented since this will increase the chances of infection. Besides, patients often infected by onychomycosis in swimming pool, gym and other public places since fungus typically concentrated on the floors of these places. Thus, it is advised to clean legs and body after going to those public places. The best way to deal with Aspergillus infection is to prevent it, but that's tough because the spores are found everywhere, even in the air we breathe in. (Infoplease.com. 2011) One of the preventive measures that could be taken is wearing oxygen breathing apparatuses by workers
who have high probability getting infection of Aspergillus. We can also clear the air arriving in chambers by special air filters. (Aspergillosis, 2011) Histoplasmosis spread thru the spores in droppings of bats or birds, it is advisable wear masks while dealing with the droppings and maintain good health status since it invade human body while the immunity is low.

Prevention and Awareness

Onychomycosis is a fungal disease on nails which is hard to be prevented and can be cured by the Terbinafine. Aspergillosis usually occurs in the lung of immunocompromised patients whereas Histoplasmosis frequently spread through inhalation of spores into lungs and infects other parts of the body. Both aspergillosis and histoplasmosis can be cured by itraconazole.

References


27. Reilly, B.O., 1996. Terbinafine. NSW Therapeutic Assessment Group Inc. 1-16


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