

## Risk Factors of Aspergillosis: its Signs and Symptoms

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### DESCRIPTION

Aspergillosis is a fungal infection, usually of the lungs, caused by the genus *Aspergillus*, a common fungus that is often inhaled from ambient air but usually does not affect most people. It is generally found in people with lung diseases such as asthma, cystic fibrosis or tuberculosis, or in those who have had stem cell or organ transplants, and in those who cannot fight the infection because of the medicines they are taking, such as steroids and some cancer treatment. It can rarely affect the skin.

Aspergillosis occurs in humans, birds and other animals. Aspergillosis occurs in chronic or acute forms, which are clinically very different. Most cases of acute aspergillosis occur in people with severely compromised immune systems, such as those undergoing bone marrow transplants. Chronic colonization or infection can cause complications in people with underlying respiratory disease such as asthma, cystic fibrosis, sarcoidosis, tuberculosis or chronic obstructive pulmonary disease. Aspergillosis most often occurs in the form of Chronic Pulmonary Aspergillosis (CPA), Aspergilloma or Allergic Bronchopulmonary Aspergillosis (ABPA). Some forms intertwine; for example, ABPA and simple aspergilloma can progress to chronic pulmonary aspergillosis [1].

Other, non-invasive manifestations include fungal sinusitis (both allergic in nature and with embedded fungal balls), otomycosis (ear infection), keratitis (eye infection) and onychomycosis (nail infection). In most cases, they are less severe and can be treated with effective antifungal therapy.

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The most commonly identified pathogens are *Aspergillus fumigatus* and *Aspergillus flavus*, ubiquitous organisms capable of living under extensive environmental stress. It is thought that most people inhale thousands of *Aspergillus* spores daily, but without effect due to an effective immune response. Overall, the major chronic, invasive, and allergic forms of aspergillosis account for approximately 600,000 deaths annually worldwide [4].

### Risk factors

Immunocompromised people, such as patients undergoing hematopoietic stem cell transplantation, chemotherapy for leukemia, or AIDS, are at increased risk of invasive aspergillosis infections. These people may have neutropenia or corticoid-induced immunosuppression as a result of medical treatment. Neutropenia is often caused by extremely cytotoxic drugs such as cyclophosphamide [5]. Cyclophosphamide interferes with cell replication, including that of white blood cells such as neutrophils. A reduced number of neutrophils inhibits the body's ability to mount immune responses against pathogens [6]. Although tumor necrosis factor alpha (TNF- $\alpha$ ), a signaling molecule associated with acute inflammatory responses, is produced, the abnormally low number of neutrophils present in neutropenic patients leads to a depressed inflammatory response.

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If the underlying neutropenia is not fixed, rapid and uncontrolled growth of invasive fungal hyphae will occur, leading to negative health outcomes. In addition to reduced neutrophil degranulation, the antiviral response against influenza and SARS-CoV-2 viruses, mediated by type I and type II interferon, is reduced together with the local antifungal immune response measured in the lungs of patients with IAPA (Influenza-Associated Pulmonary Aspergillosis) and CAPA (Pulmonary Aspergillosis associated with COVID-19).

### Signs and symptoms

A fungus ball in the lungs may cause no symptoms and may only be discovered with a chest X-ray, or it may cause repeated coughing up of blood, chest pain, and occasionally severe, even fatal, bleeding. A rapidly invasive *Aspergillus* infection in the lungs often causes cough, fever, chest pain, and difficulty breathing [7].

Poorly controlled aspergillosis can spread through the blood and cause extensive organ damage. Symptoms include fever, chills, shock, delirium, seizures and blood clots. A person may develop kidney failure, liver failure (causing jaundice) and breathing problems. Death can happen quickly.

Aspergillosis of the ear canal causes itching and sometimes pain. Fluid leaking from the ear overnight can leave a stain on the pillow. Sinus aspergillosis causes a feeling of congestion and sometimes pain or discharge. It may extend beyond the sinuses [8].

In addition to symptoms, an X-ray or Computed Tomography (CT) scan of the infected area provides clues to the diagnosis.

Whenever possible, the doctor will send a sample of the infected material to a laboratory to confirm the identification of the fungus.

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