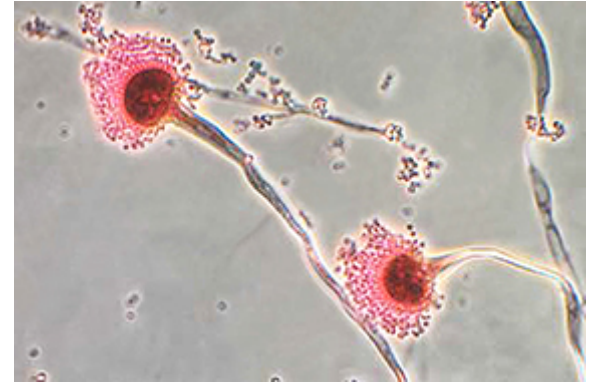


# Fungal Diseases

## Sources of Aspergillosis

### *Aspergillus* lives in the environment

*Aspergillus*, the mold (a type of fungus) that causes aspergillosis, is very common both indoors and outdoors, so most people breathe in fungal spores every day. It's probably impossible to completely avoid breathing in some *Aspergillus* spores. For people with healthy immune systems, breathing in *Aspergillus* isn't harmful. However, for people who have weakened immune systems, breathing in *Aspergillus* spores can cause an infection in the lungs or sinuses which can spread to other parts of the body.



Photomicrograph of *Aspergillus fumigatus*

### I'm worried that the mold in my home is *Aspergillus*. Should someone test the mold to find out what it is?

No. Generally, it's not necessary to identify the species of mold growing in a home, and CDC doesn't recommend routine sampling for molds. For more information about indoor mold, including cleanup and remediation recommendations, please visit CDC's [Basic Facts about Mold](#) web page.

### Types of *Aspergillus*

There are approximately 180 species of *Aspergillus*, but fewer than 40 of them are known to cause infections in humans. *Aspergillus fumigatus* is the most common cause of human *Aspergillus* infections. Other common species include *A. flavus*, *A. terreus*, and *A. niger*.

**Next:** [Learn about diagnosis and testing for Aspergillosis >](#)

Page last reviewed: January 2, 2019

## Fungal Diseases

# Diagnosis and Testing for Aspergillosis

### How is aspergillosis diagnosed?

Healthcare providers consider your medical history, risk factors, symptoms, physical examinations, and lab tests when diagnosing aspergillosis. You may need imaging tests such as a chest x-ray or a CT scan of your lungs or other parts of your body depending on the location of the suspected infection. If your healthcare provider suspects that you have an *Aspergillus* infection in your lungs, he or she might collect a sample of fluid from your respiratory system to send to a laboratory. Healthcare providers may also perform a tissue biopsy, in which a small sample of affected tissue is analyzed in a laboratory for evidence of *Aspergillus* under a microscope or in a fungal culture. A blood test can help diagnose invasive aspergillosis early in people who have severely weakened immune systems.

**Next:** [Learn about treatment for Aspergillosis >](#)

Page last reviewed: January 2, 2019

## Fungal Diseases


# Treatment for Aspergillosis

### Allergic forms of aspergillosis

For allergic forms of aspergillosis such as allergic bronchopulmonary aspergillosis (ABPA) or allergic *Aspergillus* sinusitis, the recommended treatment is itraconazole, a prescription antifungal medication. Corticosteroids may also be helpful.

### Invasive aspergillosis

Invasive aspergillosis needs to be treated with prescription antifungal medication, usually voriconazole. Other antifungal medications used to treat aspergillosis include lipid amphotericin formulations, posaconazole, isavuconazole, itraconazole, caspofungin, and micafungin. Whenever possible, immunosuppressive medications should be discontinued or decreased. People who have severe cases of aspergillosis may need surgery. Other invasive forms of aspergillosis such as chronic pulmonary aspergillosis and cutaneous aspergillosis should be treated similarly to invasive aspergillosis. Aspergillomas (“fungus ball”) might not need treatment.

If you are a healthcare provider, click here to see the Infectious Diseases Society of America’s [Practice Guidelines for the Diagnosis and Management of Aspergillosis](#) .

**Next:** [Information for healthcare professionals about Aspergillosis >](#)

Page last reviewed: January 2, 2019

# Fungal Diseases

## Information for Healthcare Professionals about Aspergillosis

### Clinical features

In immunosuppressed hosts: invasive pulmonary infection, usually with fever, cough, and chest pain. Infection may disseminate to other organs, including brain, skin and bone.

In immunocompetent hosts: Localized pulmonary infection in people with underlying lung disease, allergic bronchopulmonary disease, and allergic sinusitis.

### Etiologic agent

Most commonly, *Aspergillus fumigatus* and *A. flavus*. Less common species include *A. terreus*, *A. nidulans*, *A. niger*, and *A. versicolor*.

### Reservoir

*Aspergillus* is ubiquitous in the environment; it can be found in soil, decomposing plant matter, household dust, building materials, plants, food, and water.

### Transmission

Transmission occurs through inhalation of airborne conidia. Hospital-acquired infections may be sporadic or may be associated with dust exposure during building renovation or construction. Occasional outbreaks of cutaneous infection have been traced to contaminated biomedical devices. The incubation period for aspergillosis is unclear and likely varies depending on the dose of *Aspergillus* and the host immune response.

[CDC's Healthcare Infection Control Practices Advisory Committee \(HICPAC\) has developed guidelines](#) for environmental infection control.

### Diagnosis

A definitive diagnosis of aspergillosis typically requires a positive culture from a normally sterile site and histopathological evidence of infection. Other diagnostic tools include radiology, galactomannan antigen detection, Beta-D-glucan detection, and polymerase chain reaction (PCR).

- **Microscopy:** Evaluation of respiratory specimens after the application of special stains can allow for visualization of *Aspergillus* elements. They appear as septated hyphae with acute angle branching. However, definitive identification is difficult to make by this method alone as it is insensitive and even when positive, several filamentous fungi have a similar microscopic appearance.
- **Histopathology:** Important for documentation of invasive disease. Similar to microscopy, *Aspergillus* appears as septated hyphae with acute angle branching and can be mistaken for other filamentous molds.
- **Culture:** Can be done on a variety of sterile specimens and *Aspergillus* spp. present as rapidly growing molds that are visible 1-3 days after incubation. Culture allows for the microscopic identification down to the species level; however, this method is relatively insensitive, so patients with invasive aspergillosis may have negative cultures.
- **Galactomannan antigen test:** This test detects a polysaccharide that makes up part of the cell wall of *Aspergillus* spp. and other fungi. The Platelia (Bio-Rad Laboratories) assay is approved by the US Food and Drug Administration (FDA) for serum and bronchoalveolar lavage fluid. False positive tests have been reported in association with administration of certain antibiotics and cross reactivity exists with other fungal infections, such as those due to *Fusarium* spp. or *Histoplasma capsulatum*.
- **Beta-d-glucan assay:** This test also detects a component in the cell wall of *Aspergillus* spp, as well as other fungi. The Fungitell® assay has been approved by the FDA for diagnosis of invasive fungal infections, including those due to *Aspergillus*, *Candida*, and *Pneumocystis*. Similar to galactomannan testing, the specificity of this assay is reduced in a variety of clinical settings, including exposure to certain antibiotics, hemodialysis, and co-infection with certain bacteria.
- **Polymerase Chain Reaction (PCR):** PCR for detection of *Aspergillus* spp. from clinical specimens, including tissue and bronchoalveolar lavage fluid, is offered by some laboratories.

# Treatment and antifungal resistance

## Treatment

First-line treatment for invasive aspergillosis is voriconazole. Alternative treatments include lipid amphotericin formulations, posaconazole, isavuconazole, itraconazole, caspofungin, and micafungin. Prophylaxis against aspergillosis is recommended during prolonged neutropenia for patients who are at high risk for aspergillosis, allogeneic stem cell transplant patients with graft versus host disease, lung transplant recipients, and certain other solid organ transplant recipients under certain conditions.

For more detailed recommendations on treatment and prophylaxis, please refer to the Infectious Diseases Society of America's [Practice Guidelines for the Diagnosis and Management of Aspergillosis](#) [↗](#).

## Antifungal resistance

Even with antifungal treatment, aspergillosis can cause death in more than half of infected patients with weakened immune systems. Infections with resistant strains of *Aspergillus fumigatus* can be even harder to treat. Some *A. fumigatus* strains carry resistance markers that have been associated with environmental fungicide use rather than previous patient exposure to antifungals. *Aspergillus fumigatus* resistant to all azole antifungal medications (including voriconazole, itraconazole, and posaconazole) is emerging in the United States <sup>1,2,3</sup> and clinicians and public health personnel should be aware that resistant infections are possible even in patients not previously exposed to these medications. Further research is needed to determine how widespread this resistance is.

For more detailed information on antifungal resistant *Aspergillus fumigatus*, please see the CDC [Antifungal Resistance](#) page.

## Risk groups

Risk groups for invasive aspergillosis include persons who have severe/prolonged granulocytopenia, hematologic malignancies, receipt of a hematopoietic stem cell or solid organ transplant, and high-dose corticosteroids or other immunosuppressive therapies.

Risk groups for allergic aspergillosis include persons who have asthma, cystic fibrosis, or other underlying lung diseases.

## Surveillance and statistics

Aspergillosis is not a reportable infection. [Click here for aspergillosis statistics](#).

## Areas for further research

- Developing more sensitive and specific methods for earlier diagnosis
- Improving our understanding of environmental sources and routes of transmission
- Improved availability of advanced molecular typing methods to assist in epidemiologic studies
- Developing surveillance for resistant *Aspergillus* infections

# Improving our understanding of invasive aspergillosis among patients with severe influenza

## The Concern

Aspergillosis usually occurs in people with severely weakened immune systems. However, several reports describe *Aspergillus* lung infections that caused death in previously healthy patients who were hospitalized for severe illness associated with influenza virus infection. The *Aspergillus* infections involved pneumonia or severe tracheobronchitis (infection of the lung's airways) <sup>4-6</sup>. A retrospective cohort study at seven intensive care units (ICU) in Belgium and the Netherlands found that invasive pulmonary aspergillosis occurred in 19% of patients with severe influenza requiring admission to the ICU. Approximately half of the patients with invasive pulmonary aspergillosis and severe influenza did not have an immunocompromising condition <sup>7</sup>.

Severe lung infections caused by influenza and other viruses can damage the respiratory epithelium (or lining of the lung). Some researchers suspect that this damage can allow *Aspergillus* to invade and cause infection <sup>8</sup>. This process may be similar to how some bacteria, for example *Streptococcus pneumoniae* and *Staphylococcus aureus*, cause pneumonia in patients with severe illness associated with influenza virus infections.

More research is needed to determine how commonly these types of *Aspergillus* infections occur among influenza patients with functioning immune systems and in those who are severely immunocompromised in countries other than the Netherlands and Belgium. Another question is whether previously healthy patients who have severe lung infections caused by viruses other than influenza virus get invasive aspergillosis.



# Testing for *Aspergillus* in Patients with Severe Lung Infections




Several types of tests may be helpful in diagnosing aspergillosis in patients with severe lung infections caused by influenza and other respiratory viruses. *Aspergillus* can be cultured from patient samples taken by bronchoalveolar lavage (a rinse of the lung's airways using a specialized device). These samples can also be tested using a galactomannan antigen test, although this test can sometimes be falsely positive or negative. Biopsies, or tissue samples, of the lung can be used to detect *Aspergillus*. Note that *Aspergillus* fungi can sometimes be found in the lung airways of patients who do not have an *Aspergillus* infection (a situation called colonization). Patients with *Aspergillus* colonization, but without a weakened immune system or other typical risk factors, can develop severe *Aspergillus* infections when critically ill<sup>9</sup> and show evidence of invasive aspergillosis<sup>4,10</sup>.

## Vigilance for Aspergillosis

Influenza viral pneumonitis, or bacterial co-infection secondary to influenza can lead to respiratory failure, sepsis, and multi-organ failure. Healthcare providers should continue to consider *Aspergillus* infection in critically ill patients with influenza who are severely immunocompromised or who received corticosteroids. Recent studies suggest that healthcare providers may also consider *Aspergillus* infection as a possible cause of worsening respiratory function and sepsis in critically ill immunocompetent patients with severe influenza<sup>7</sup>.

For any questions, please contact CDC at [aspergillus@cdc.gov](mailto:aspergillus@cdc.gov).

## References

1. Fisher MC, Hawkins NJ, Sanglard D, Gurr SJ. Worldwide emergence of resistance to antifungal drugs challenges human health and food security. *Science*. 2018 May; 360(6390): 739-742.
2. Verweij PE, Chowdhary A, Melchers WJ, Meis JF. Azole resistance in *Aspergillus fumigatus*: Can we retain the clinical use of mold-active antifungal azoles? *Clin Infect Dis*. 2016 Feb 1;62(3): 362-368.
3. Beer KD, et al. Multidrug-resistant *Aspergillus fumigatus* carrying mutations linked to environmental fungicide exposure — three states, 2010–2017. *MMWR* 2018 Sept 28; 67(38): 1064–1067.
4. Van de Veerdonk FL, Kolwijck E, Lestrade PPA, Hodiament CJ, Rijnders BJA, van Paassen J, et al. Influenza-associated aspergillosis in critically ill patients. *Am J Respir Crit Care Med*. 2017 Apr 7;196(4):524–7.
5. Alshabani K, Haq A, Miyakawa R, Palla M, Soubani AO. Invasive pulmonary aspergillosis in patients with influenza infection: report of two cases and systematic review of the literature. *Expert Rev Respir Med*. 2015 Jan 2;9(1):89–96.
6. Wauters J, Baar I, Meersseman P, Meersseman W, Dams K, Paep RD, et al. Invasive pulmonary aspergillosis is a frequent complication of critically ill H1N1 patients: a retrospective study. *Intensive Care Med*. 2012 Nov 1;38(11):1761–8.
7. Schauwvlieghe AFAD, Rijnders BJA, Philips N, Verwijs R, Vanderbeke L, Tienen CV, et al. Invasive aspergillosis in patients admitted to the intensive care unit with severe influenza: a retrospective cohort study. *Lancet Respir Med* [Internet]. 2018 Jul 31 [cited 2018 Aug 1];0(0). Available from: [https://www.thelancet.com/journals/lanres/article/PIIS2213-2600\(18\)30274-1/abstract](https://www.thelancet.com/journals/lanres/article/PIIS2213-2600(18)30274-1/abstract) 
8. Crum-Cianflone NF. Invasive aspergillosis associated with severe influenza infections. *Open Forum Infect Dis* [Internet]. 2016 May 1 [cited 2018 Jan 27];3(3). Available from: <https://academic.oup.com/ofid/article/3/3/ofw171/2593326> 
9. Shah MM, Hsiao EI, Kirsch CM, Gohil A, Narasimhan S, Stevens DA. Invasive pulmonary aspergillosis and influenza co-infection in immunocompetent hosts: case reports and review of the literature. *Diagn Microbiol Infect Dis* [Internet]. 2018 Feb 2 [cited 2018 Mar 28]; Available from: <http://www.sciencedirect.com/science/article/pii/S0732889318300191> 
10. Lat A, Bhadelia N, Miko B, Furuya EY, Thompson GR. Invasive aspergillosis after pandemic (H1N1) 2009. *Emerg Infect Dis*. 2010 Jun;16(6):971–3.

# Fungal Diseases

## Aspergillosis Statistics

### How common is aspergillosis?

Because aspergillosis is not a reportable infection in the United States, the exact number of cases is difficult to determine. Milder, allergic forms of aspergillosis are more common than the invasive form of the infection.

Allergic bronchopulmonary aspergillosis (ABPA) likely affects between 1 and 15% of cystic fibrosis patients.<sup>1</sup> One study calculated that 2.5% of adults who have asthma also have ABPA, which is approximately 4.8 million people worldwide.<sup>2</sup> Of these 4.8 million people who have ABPA, an estimated 400,000 also have chronic pulmonary aspergillosis (CPA).<sup>2</sup> Another 1.2 million people are estimated to have CPA after having tuberculosis,<sup>3</sup> and over 70,000 people are estimated to have CPA as a complication of sarcoidosis.<sup>4</sup>

Invasive aspergillosis is uncommon and occurs primarily in immunocompromised people. The first population-based incidence estimates for invasive aspergillosis were obtained from laboratory surveillance conducted in the San Francisco Bay Area during 1992-1993 and suggested a yearly rate of 1 to 2 cases of aspergillosis per 100,000 population.<sup>5</sup> However, the epidemiology of invasive *Aspergillus* infections has likely shifted since this time due to the increasing number of solid organ and stem cell transplant recipients and newer immunosuppressive agents. The number of hospitalizations related to invasive aspergillosis in the United States increased an average of 3% per year during 2000-2013.<sup>6</sup> Nearly 15,000 aspergillosis-associated hospitalizations occurred in the United States in 2014, at an estimated cost of \$1.2 billion.<sup>7</sup>

Prospective surveillance among transplant recipients performed during 2001-2006 found that invasive aspergillosis was the most common type of fungal infection among stem cell transplant recipients<sup>8</sup> and was the second-most common type of fungal infection among solid organ transplant recipients.<sup>9</sup> In a broad US healthcare network of intensive care unit autopsy studies, aspergillosis was one of the top four most common diagnoses that likely lead to death.<sup>10</sup>

### Aspergillosis outbreaks

Although most cases of aspergillosis are sporadic (not part of an outbreak), outbreaks of invasive aspergillosis occasionally occur in hospitalized patients. Invasive aspergillosis outbreaks are often found to be associated with hospital construction or renovation, which can increase the amount of airborne *Aspergillus*, resulting in respiratory infections or surgical site infections in high-risk patients.<sup>12,13</sup> Outbreaks of primary cutaneous aspergillosis and central nervous system aspergillosis in association with the use of contaminated medical devices have also been described.<sup>14,15</sup> The incubation period for aspergillosis is unclear and likely varies depending on the dose of *Aspergillus* and the host immune response.

### Deaths due to aspergillosis

Allergic forms of aspergillosis such as allergic bronchopulmonary aspergillosis (ABPA) and allergic *Aspergillus* sinusitis are generally not life-threatening.

In contrast, although invasive aspergillosis is uncommon, it is a serious infection and can be a major cause of mortality in immunocompromised patients. For example, a large prospective study found that the one-year survival for people who had invasive aspergillosis was 59% among solid organ transplant recipients<sup>10</sup> and 25% among stem cell transplant recipients.<sup>8</sup> In a systematic review of intensive care unit autopsy studies, aspergillosis was one of the top four most common diagnoses that likely lead to death.<sup>11</sup>

### References

1. Stevens DA, Moss RB, Kurup VP, Knutsen AP, Greenberger P, Judson MA, et al. Allergic bronchopulmonary aspergillosis in cystic fibrosis—state of the art: Cystic Fibrosis Foundation Consensus Conference. *Clin Infect Dis*. 2003 Oct 1;37 Suppl 3:S225-64.
2. Denning DW, Pleuvry A, Cole DC. Global burden of allergic bronchopulmonary aspergillosis with asthma and its complication chronic pulmonary aspergillosis in adults. *Med Mycol*. 2013 May;51(4):361-70.
3. Denning DW, Pleuvry A, Cole DC. Global burden of chronic pulmonary aspergillosis as a sequel to pulmonary tuberculosis. *Bull World Health Organ*. 2011 Dec 1;89(12):864-72.
4. Denning DW, Pleuvry A, Cole DC. Global burden of chronic pulmonary aspergillosis complicating sarcoidosis. *Eur Respir J*. 2013

5. Rees JR, Pinner RW, Hajjeh RA, Brandt ME, Reingold AL. The epidemiological features of invasive mycotic infections in the San Francisco Bay area, 1992-1993: results of population-based laboratory active surveillance. *Clin Infect Dis*. 1998 Nov;27(5):1138-47.
6. Vallabhaneni S, Benedict K, Derado G, Mody RK. Trends in Hospitalizations Related to Invasive Aspergillosis and Mucormycosis in the United States, 2000-2013. *Open Forum Infect Dis*. 2017 Winter;4(1):ofw268.
7. Benedict K, Jackson BR, Chiller T, Beer KD. Estimation of direct healthcare costs of fungal diseases in the United States. *Clin Infect Dis*. 2018 Sep 10.
8. Kontoyiannis DP, Marr KA, Park BJ, Alexander BD, Anaissie EJ, Walsh TJ, et al. Prospective surveillance for invasive fungal infections in hematopoietic stem cell transplant recipients, 2001-2006: overview of the Transplant-Associated Infection Surveillance Network (TRANSNET) Database. *Clin Infect Dis*. 2010 Apr 15;50(8):1091-100.
9. Pappas PG, Alexander BD, Andes DR, Hadley S, Kauffman CA, Freifeld A, et al. Invasive fungal infections among organ transplant recipients: results of the Transplant-Associated Infection Surveillance Network (TRANSNET). *Clin Infect Dis*. 2010 Apr 15;50(8):1101-11.
10. Webb BJ, Ferraro JP, Rea S, Kaufusi S, Goodman BE, Spalding J. Epidemiology and Clinical Features of Invasive Fungal Infection in a US Health Care Network. *Open Forum Infect Dis* 2018 Jul 31;5(8):ofy187.
11. Winters B, et al. Diagnostic errors in the intensive care unit: a systematic review of autopsy studies. *BMJ Qual Saf*. 2012 Nov;21(11):894-902.
12. Weber DJ et al. Preventing healthcare-associated *Aspergillus* infections: a review of recent CDC/HICPAC recommendations. *Med Mycol* 2009; 47S1: S199-209
13. Vonberg RP, Gastmeier P. Nosocomial aspergillosis in outbreak settings. *J Hosp Infect*. 2006 Jul;63(3):246-54.
14. Allo MD, Miller J, Townsend T, Tan C. Primary cutaneous aspergillosis associated with Hickman intravenous catheters. *N Engl J Med*. 1987 Oct 29;317(18):1105-8.
15. Gunaratne PS, Wijeyaratne CN, Seneviratne HR. *Aspergillus meningitis* in Sri Lanka—a post-tsunami effect? *N Engl J Med*. 2007 Feb 15;356(7):754-6.