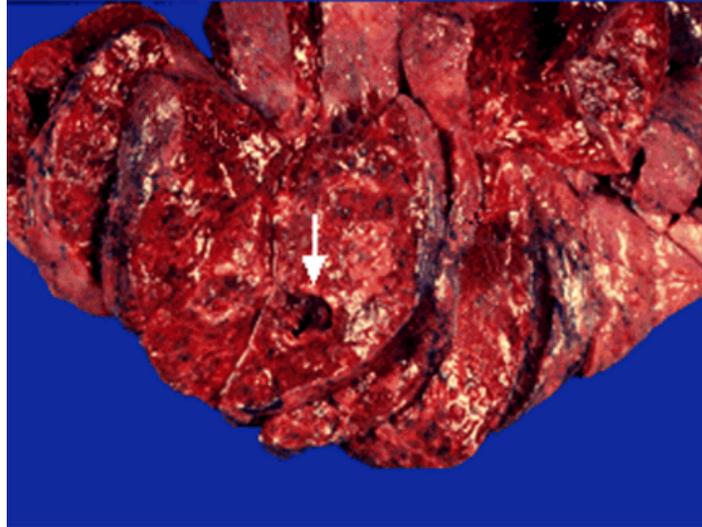


Aspergillosis (sourced from the internet)



Aspergillus hyphae in lung invading blood vessels

Contamination of building substrates with fungi, particularly *Aspergillus* species have become an increasing concern. Aspergillosis is now the second most common fungal infection requiring hospitalization in the United States.

Many people with damaged or impaired immune systems die from invasive aspergillosis. Their chances of living are improved the earlier the diagnosis is made but unfortunately there is no good single diagnostic test. Often treatment has to be started when the condition is only suspected.

Half to two thirds of patients die from invasive aspergillosis even if treated, and none survive if they are not treated. *A. fumigatus* causes more infections worldwide than any other mould. 4% of all patients dying in tertiary care hospitals in Europe have invasive aspergillosis.

There has been substantial increase in populations of individuals with active immune suppression, such as individuals that have had bone marrow or organ transplants, patients with neutropenia, neutrophil or macrophage dysfunction, chemotherapy patients, burn victims, malnourished children, influenza, TB, asthma, kidney failure requiring dialysis, diabetes, those that take drugs that suppress the immune system, and those on corticosteroid treatment.

Aspergillus

What is it?

Aspergillus is a group of moulds, which is found everywhere world-wide, especially in the autumn and winter in the Northern hemisphere. Moulds are also called filamentous fungi. Only a few of these moulds can cause illness in humans and animals. Most people are naturally immune and do not develop disease caused by *Aspergillus*. However, when disease does occur, it takes several forms.

The types of diseases caused by *Aspergillus* are varied, ranging from an allergy-type illness to life-threatening generalised infections. Diseases caused by *Aspergillus* are called aspergillosis. The severity of aspergillosis is determined by various factors but one of the most important is the state of the immune system of the person.

Allergic bronchopulmonary aspergillosis (ABPA)

This is a condition, which produces an allergy to the spores of the *Aspergillus* moulds. It is quite common in asthmatics; up to 5% of adult asthmatics might get this at some time during their lives. ABPA is also common in cystic fibrosis patients, as they reach adolescence and adulthood. The symptoms are similar to those of asthma: intermittent episodes of feeling unwell, coughing and wheezing. Some patients cough up brown-coloured plugs of mucus. The diagnosis can be made by X-ray or by sputum, skin and blood tests. In the long term ABPA can lead to permanent lung damage (fibrosis) if untreated.

The treatment is with steroids by aerosol or mouth (prednisolone), especially during attacks. Itraconazole (an oral antifungal drug) is useful in reducing the amount of steroids required in those needing medium or high doses. This is beneficial as steroids have side-effects like thinning of the bones (osteoporosis) and skin and weight gain, especially when used for a long time. It is not known whether patients with ABPA not on steroids (or on low doses) benefit in some way.

Aspergilloma and chronic pulmonary aspergillosis

This is a very different disease also caused by the *Aspergillus* mould. The fungus grows within a cavity of the lung, which was previously damaged during an illness such as tuberculosis or sarcoidosis. Any lung disease which causes cavities can leave a person open to developing an aspergilloma. The spores penetrate the cavity and germinate, forming a fungal ball within the cavity. In some people, cavities in the lung are formed by *Aspergillus*, and no fungal ball is present. The fungus secretes toxic and allergic products, which may make the person feel ill.

The person affected may have no symptoms (especially early on). Weight loss, chronic cough, feeling rundown and tired are common symptoms later. Coughing of blood (haemoptysis) can occur in up to 50-80% of affected people.

The diagnosis is made by X-rays, scans of lungs and blood tests.

Treatment depends on many factors including whether the patient is coughing blood and how much lung disease there is. Those with no symptoms may need no treatment. Oral itraconazole (usually 400 mg daily) helps symptoms in many patients but rarely kills the fungus in the cavity. A new alternative is voriconazole, which is at least as effective as itraconazole. Sometimes surgical removal is possible, especially if the patient is coughing blood. Surgery is difficult however, and therefore is best reserved for single lung cavities. Sometimes other antifungal drugs (especially amphotericin B) can be injected directly into the cavity by a tube, which is put into position under local anaesthesia.

Aspergillus sinusitis

Aspergillus disease can happen in the sinuses leading to *Aspergillus* sinusitis. Just as in the lungs, *Aspergillus* can cause the three diseases - allergic sinusitis, a fungal ball or invasive aspergillosis.

Allergic disease is associated with long standing symptoms of a runny blocked up nose, and may lead to nasal polyps. Surgical drainage, including removal of polyps, careful attention to treatment of bacterial infection, local steroids and/or short courses of oral steroids and antifungals applied locally are the approaches to therapy.

The fungal ball caused by *Aspergillus* happens in a similar way to an aspergilloma. In those with normal immune systems, stuffiness of the nose, chronic headache or discomfort in the face is common. Drain-

age of the sinus, by surgery, usually cures the problem, unless the *Aspergillus* has entered the sinuses deep inside the skull. Then antifungal drugs and surgery is usually successful.

When patients have damaged immune systems - if, for example they have had leukaemia or have had a bone marrow transplant - *Aspergillus* sinusitis is more serious. In these cases the sinusitis is a form of invasive aspergillosis. The symptoms include fever, facial pain, nasal discharge and headaches. The diagnosis is made by finding the fungus in fluid or tissue from the sinuses and with scans. Surgery is done in most cases as it is important to find out what is exactly wrong and is often helpful in eradicating the fungus. Treatment with powerful antifungal medicines is essential. Choices of treatment include amphotericin B, caspofungin, voriconazole or itraconazole. Response may be better to amphotericin B than voriconazole or itraconazole; the role of caspofungin is uncertain, as there is little experience.

Invasive aspergillosis

Many people with damaged or impaired immune systems die from invasive aspergillosis. Their chances of living are improved the earlier the diagnosis is made but unfortunately there is no good single diagnostic test. Often treatment has to be started when the condition is only suspected.

This condition is usually clinically diagnosed in a person with low defences such as bone marrow transplant, low white cells after cancer treatment, AIDS or major burns. There is also a rare inherited condition that gives people low immunity (chronic granulomatous disease) which puts affected people at moderate risk. People with invasive aspergillosis usually have a fever and symptoms from the lungs (cough, chest pain or discomfort or breathlessness) which do not respond to standard antibiotics. X-rays and scans are usually abnormal and help to localise the disease. Bronchoscopy (inspection of the inside of the lung with a small tube inserted via the nose) is often used to help to confirm the diagnosis. Cultures and blood tests are usually necessary to confirm the disease.

In people with particularly poor immune systems, the fungus can transfer from the lung through the blood stream to the brain or to other organs, including the eye, the heart, the kidneys and the skin. Usually this is a bad sign as the condition is more severe and the person sicker with a higher risk of death. However, sometimes infection of the skin enables the diagnosis to be made earlier and treatment to be started sooner.

Treatment is with antifungal drugs such as [voriconazole](#), [caspofungin](#), [itraconazole](#) or [amphotericin B](#). Voriconazole is usually better than amphotericin B. Some other drugs used for the treatment of tuberculosis or epilepsy reduce the blood levels of voriconazole. Voriconazole can be given orally or intravenously. It is better than amphotericin B, but may require dose modification to maximise success, especially in children, those with liver disease or cirrhosis and possibly the elderly.

Caspofungin can only be given intravenously, and is also partially effective. It has been used as rescue therapy and in combination with other antifungals, with reasonable success.

Amphotericin B has to be given by vein in large doses. In some patients the treatment can damage the kidney and other organs. Newer forms of amphotericin B (Amphotec or Amphocil, Abelcet or AmBisome) are useful, especially when the patient experiences side-effects, as they usually cause fewer side effects, especially less renal dysfunction.

Itraconazole is generally given orally (also in large doses, e.g. at least 400 mg daily), although an intravenous preparation is available now. Itraconazole is often used for follow on therapy.

The earlier treatment is started the better the chances of survival. In patients with low numbers of white cells (infection fighters), recovery of these cells can be important in stopping the growth of the fungus. Sometimes surgery is also required. Overall, a third to a half of patients survive invasive aspergillosis if

treated and none survive if they are not treated.

All these conditions can affect children and should be diagnosed and treated in the same way. A lot of encouraging research is being done at the moment to speed up diagnosis of this invasive aspergillosis and to improve its treatment. Some new antifungal drugs (posaconazole, micafungin and anidulafungin in particular) are in clinical trials at present.

Addendum

The most frequently encountered opportunistic *Aspergillus* pathogen, *Aspergillus fumigatus*, is seen most abundantly in decomposing organic materials. Because it grows well at temperatures up to 55°C, self-heating compost piles provide an excellent environment for the fungi. Compost made up of chipped branches and leaves will often yield a massive and virtually pure culture of *A. fumigatus*. *A. fumigatus* has been reported to be the major organism isolated from air samples obtained near compost sites. People who handle compost or decomposing haystacks often develop hypersensitivity to spores of *Aspergillus* and after exposure may suffer a severe allergic response.

Aspergillus flavus is the second most frequently encountered fungi in cases of infection with *Aspergillus* species. In addition to causing infections, *Aspergillus flavus* is also renowned for its production of aflatoxin, one of the most potent carcinogens known to man. Concern about aflatoxin began in the 1960's after some 100,000 turkey poults in Great Britain died as a result of ingesting feed tainted with aflatoxin. When it became evident that aflatoxin was highly carcinogenic most industrialized countries established tolerances for aflatoxin levels in food and feeds. The risks associated with airborne exposure to aflatoxin in contaminated buildings, as with other mycotoxins, have not been adequately studied.