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Aspergillosis

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Aspergillus species are ubiquitous in nature, particularly in decaying vegetation, such as in piles of leaves or compost piles. Building work, including that performed in hospitals, may release copious quantities of spores into the air. There are more than 100 species within the genus but only a few have been regularly implicated in human disease: *Aspergillus fumigatus* and *A. flavus* are the most common causes of aspergillosis, although other species have also been implicated.

Invasive aspergillosis may occur, particularly in patients receiving cytotoxic or immunosuppressive therapy; it may disseminate usually from the lung to the brain, kidneys and other organs, and is often fatal. *A. fumigatus* causes most cases of fungus ball; *A. niger* is the usual cause of fungal otitis externa. Aspergillosis most frequently affects the lungs, but infections at other sites such as the nasal sinuses and superficial tissues may also occur. Inhalation of aspergillus spores may lead to colonisation of bronchial mucosa or existing lung cavities, or a hypersensitivity reaction. These organisms may also infect the implantation site of a cardiac prosthetic valve. Growing on certain foods, many isolates of *A. flavus* will produce aflatoxins or other mycotoxins; these cause disease in animals and fish and are highly carcinogenic for experimental animals. An association between high aflatoxin levels in foods and hepatocellular cancer in man has been noted in Africa and Southeast Asia[1].

The value of the laboratory diagnosis varies according to the clinical form of aspergillosis; the diagnosis of invasive disease is particularly difficult. All of the aspergilli grow well on routine mycological laboratory media, commonly forming distinctively-coloured colonies. They form mycelia, and also spore heads which are typical for the different species and hence the species identification made by microscopical examination. Since aspergillus spores are ubiquitous, it is frequently difficult, when they are isolated from pathological material, to determine whether they bear any aetiological relationship to the infectious condition. The presence of aspergilli is not sufficient to diagnose an infection. The growth of an aspergillus colony on a culture plate may reflect no more than aerial contamination in the laboratory or mere colonisation of a body surface. Histological demonstration of hyphae infiltrating a tissue demonstrates invasive disease. Multiple colonies grown from a single specimen, and repeated isolation of the same species from different samples) also help to establish clinical significance.

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Immunologic tests such as demonstration of IgG and IgE antibodies as well as positive skin reactions have long been used in the diagnosis of various clinical forms of aspergillosis. Many serologic tests have been developed with variable sensitivities to detect circulating antibodies. These tests have proven useful in the diagnosis of allergic aspergillosis and aspergilloma, but not in the diagnosis of invasive disease. Antibody production against aspergilli may not be seen in immunosuppressed patients, in part due to the nature of their underlying conditions and also perhaps as a result of antifungal therapy or following fulminant aspergillus infections. In invasive disease, antigen detection may be occasionally helpful to establish an early diagnosis. Also monitoring levels of antigens may be useful for the management of patients, especially those with immunosuppression or malignancies. However, it has been demonstrated that currently available antibody assays of invasive disease are inadequate; antigen detection tests are highly specific but lack sufficient sensitivity to be of practical use in the clinical laboratory[2].

A variety of tests for the detection of soluble antigens of *Aspergillus* species in body fluids have been developed. These methods may provide sensitivity sufficient to allow early diagnosis in some cases, but few are commercially available[3]. Methods for the detection of antigenaemia have been recently summarised. Regardless of the test used, success in detecting antigenaemia is directly related to the frequency of monitoring of samples[4].

Skin tests have been used in patients with allergic bronchopulmonary aspergillosis (ABPA), atopic dermatitis or allergic asthma sensitised to aspergilli. Recombinant allergens that can be produced as highly pure proteins may contribute significantly to the improvement in the diagnosis of ABPA[5].

Some *Aspergillus* species produce large amounts of 6-carbon polyol mannitol in culture, and infected animals with invasive disease have been shown to have high body fluid and tissue mannitol levels. Routine use of this method has been hampered by the need for complex analytical methods[6].

The sensitivity and specificity of molecular techniques make them attractive as alternative methods for the early diagnosis of invasive aspergillosis, but they are still experimental.

In summary, in the diagnosis of invasive aspergillosis, biopsy may be the only reliable method

of making a definitive diagnosis, although this procedure may not be practical because of the associated risk. All too often the diagnosis is first made at post-mortem. The diagnosis should be considered in any febrile immunocompromised patient, particularly if lung infiltrates are visible on the chest X-ray. Despite improvements in blood culture systems, this investigation is usually negative in patients with invasive aspergillosis. Improvements in antigen detection techniques would be of great utility in making this difficult diagnosis. Early diagnosis is necessary in this life-threatening condition; specific diagnosis is vital as the established therapeutic regimes are either toxic or expensive.

REFERENCES

1. Benenson AS. Control of Communicable Diseases Manual. 16th ed. American Public Health Association, 1995.
2. Manso E, Montillo M, DeSio G, D'Amico S, Decepoli G, Leoni P. Value of antigen and antibody detection in the serologoal diagnosis of invasive aspergillosis in patients with hematological malignancies. Eur J Clin Microbiol Infect Dis 1994; 13:756-60.
3. Van Cutsem J, Meulemans L, Van Gerven F, Stynen D. Detection of circulating galactomannan by Pastorex Aspergillus in experimental invasive aspergillosis Mycoses 1990; 33:61-9.
4. Wilson EV, Hearn VM, Mackenzie DWR. Evaluation of a test to detect circulating Asperillus fumigatus antigen in a survey of immunocompromised patients with proven or suspected invasive disease. J Med Vet Mycol 1987; 25:365-74.
5. Moses M, Crameri R, Brust E, Suter M, Menz G. Diagnostic value of recombinant Aspergillus fumigatus allergen I/a for skin testing and serology. J Allergy Clin Immunol 1994; 93:1-11.
6. National Institute of Allergy and Infectious Disease. NIAID Workshop on Molecular and Immunologie Approaches to the Diagnosis and Treatment of systemic Mycoses: Summary. National Institute of Allergy and Infectious Diseases, Bethesda, Md 1994.