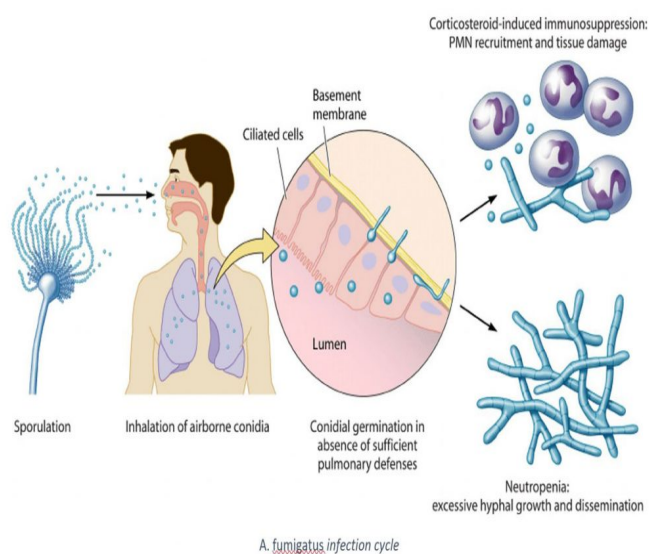


CLINICAL CONTEXT

Aspergillosis



Source : [T. Dagenais et al., 2009](#)

Aspergillosis are infections due to ubiquitous fungi of the *Aspergillus* genus. Various pathologies induced depend on several intrinsic characteristics of the fungus itself and on its host, which will condition the virulence of the disease.

Amongst hundreds of *Aspergillus* species, more than 20 are currently reported to be pathogenic for humans, but new pathogenic species are regularly identified ([Gauthier et al., 2016](#)). However, *Aspergillus fumigatus* is the most commonly encountered species of the genus. It is estimated to be responsible of more than 80% of human pathological manifestations, but this proportion varies depending on clinical forms and geographical location.

A. fumigatus is an opportunistic saprophytic pathogen, naturally present in all kind of environment (soils, air, aquatic habitats, on plants...). Extremely resistant, fungal conidia penetrates the host mostly by inhalation, but also by ingestion or cutaneous contact through wounds. As they are extremely thin, *Aspergillus* conidia can reach pulmonary alveolus. After

their endocytosis by epithelial cells of the host, they germinate and colonize by dissemination of hyphae, that can reach bloodstream and thus invade other organs ([Paulussen et al., 2017](#)).

Clinical manifestations depend on the location of the colonization, which depends on the virulence of the fungus as well as the immune response of the host. Three categories of aspergillosis are distinguished:

- Allergic reactions, including Allergic Broncho-Pulmonary Aspergillosis (ABPA). They are mainly associated with asthma, cystic fibrosis and sinusitis. They correspond to an allergic hyperreactivity to fungi, exacerbated in the case of ABPA by the growth in the pulmonary tract, leading to important inflammation of bronchi ([Denning et al., 2014](#)). Besides ABPA, allergic sensitizations are observed, in particular in association with severe asthma, farmer's lung disease or extrinsic allergic alveolitis due to massive and iterative expositions to the fungus. Allergic forms, particularly ABPA, are responsible for severe respiratory troubles among patients.
- Chronic Pulmonary Aspergillosis (CPA). Different forms are described, but they all correspond to a fungal growth, limited to a fungal ball, or aspergilloma, in the less serious forms, or with tissue invasion, necrosis and bloodstream propagation in the most serious cases. Aspergillus generally grows in a pre-existing cavity due to an underlying or past condition (mostly tuberculosis, but also after obstructive chronic broncho-pneumopathy or Kaposi sarcoma...). Without treatment, except for isolated aspergilloma, the disease has a poor prognosis ([Denning et al., 2016](#)).
- Invasive aspergillosis are the most serious forms, affecting immunosuppressed patients (in particular aplastic patients but also those in intensive care). Pulmonary forms are the most common, but disseminated forms are also described (brain, kidney, heart...) ([Latgé & Chamilos, 2019](#)). These pathologies are always lethal without treatment, and mortality remains high even with treatment.

Due to its ubiquity, infections by *Aspergillus* spp. have an important incidence worldwide. It is the first cause of fungal pulmonary infections. Chronic forms have a major impact especially for patients with tuberculosis. The WHO estimates that 22% of patients with pulmonary tuberculosis develop a CPA ([Denning et al., 2011](#)). ABPA rate among asthmatic patients is around 2,5%, reaching 7,8% for patients with cystic fibrosis ([Kanj et al., 2018](#)). Immunosuppressed patients (AIDS, grafted, hematopoietic diseases...) are at risk, especially for invasive forms, leading to a 40% mortality rate. Overall, twelve million people are suffering of severe asthma with fungal sensitization or ABPA, 3 million of a CPA form and 300.000 of invasive aspergillosis ([Bongomin et al., 2017](#)).

The diversity of aspergillosis forms implies a diversity in the diagnostic tools. For invasive aspergillosis, histopathological observation, imaging, culture, fungal DNA detection using PCR and galactomannan detection via ELISA are the most commonly used techniques ([Donnelly et al., 2020](#)).

The diagnosis of ABPA relies on a set of criteria including clinical data, total and A. fumigatus specific IgE, radiology and specific IgG ([Agarwal et al., 2013](#)).

Chronic forms of aspergillosis are diagnosed on the basis of characteristic symptoms and radiology, confirmed by microbiological immunological techniques. In most cases, precipitin or specific IgG presence indicates an Aspergillus infection. Although invasive, biopsies may be interesting, especially for the differential diagnosis of cancers ([Kanj et al., 2018](#)).

Serology, essential for the diagnosis of chronic and allergic forms, is done by several techniques. Screening is usually done by ELISA, easily automatable. Confirmation was historically performed by immuno-electrophoresis, but the lack of standardization leads the clinicians to use another technique, like Western Blot ([Persat et al., 2017](#)).

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THE ASPERGILLOSIS ICT IgG-IgM TEST

Ease of use, fast result obtention and reliability characterize the ASPERGILLOSIS ICT IgG-IgM screening test. Particularly adapted to first line laboratories and small series, this test can advantageously replace the other screening techniques ([Hunter et al., 2019](#)).

Associated with a low cost, the high specificity and sensitivity of the ASPERGILLOSIS ICT IgG-IgM benefit the patient and reduce the economic weight thanks to the establishment of a precocious and confident diagnosis ([Piarroux et al., 2019a](#)).

Several studies showed the efficacy of coupling techniques, including the ICT, to allow a precise and fast diagnosis ([Thornton, 2020](#), [Wilopo et al., 2019](#)), as well as for the follow-up of tuberculosis ([Kwizera et al., 2020](#)). The technique can be used for the diagnosis of chronic forms ([Hunter et al., 2019, 2021](#)) but also as part of ABPA diagnosis ([Hunter et al., 2020](#)).

THE ASPERGILLOSIS Western Blot IgG TEST

Studies have shown that the Western Blot performances can overcome the sensitivity and specificity of the gold standard, the immunoprecipitation, especially by giving less false negative results, in addition of the standardization of the diagnostic confirmation ([Oliva et al., 2015](#), [Persat et al., 2017](#)).

In order to meet this demand, we developed a reliable test based on the Western Blot technique. Associated with highly sensitive natural antigens, the ASPERGILLOSIS Western Blot IgG test is a robust confirmation technique of classical screening tests.

Furthermore, ongoing work are showing that the test could also be used for ABPA diagnosis by changing the conjugate used for a specific anti-IgE conjugate ([Piarroux et al., 2019b](#)).