Advancing Diagnostics and Understanding of Pulmonary Aspergillosis in Europe

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The population at risk for invasive aspergillosis has broadened mainly due to the use of new drugs in oncology and rheumatology and the recognition of the clinical entity of virus-associated pulmonary aspergillosis (VAPA). VAPA mainly occurs in ICU patients with influenza or COVID including patients with supposedly normal pre-existing immunity.

A fungal targeted diagnostic approach is needed to diagnose these infections but is complicated by the need of invasive (tissue, BAL) sampling and the difficulty to discern infection from colonisation when testing non-sterile samples. Due to the expansion of commercially available test formats, Aspergillus antigen detection and PCR tests can now be implemented in many hospitals but discordant test results (antigen/DNA) remain difficult to interpret. Aspergillus PCR tests may also be designed to detect resistance mutations in the A. fumigatus Cyp51A gene which has a clear clinical value in culture negative cases. People do inhale a mixture of azole-susceptible and azole-resistant spores which may result in genetically mixed infections further complicating the detection of triazole resistant disease in patients. Increasing triazole resistance rates in A. fumigatus is a concern, e.g. in Belgium triazole resistance rates doubled to 10% over a period of 10 years. Intriguing is the strong regional difference in triazole resistance rates.

Metagenomic next-generation sequencing expands pathogen detection and represents an adjunctive tool in complex or high-risk cases, especially in the context of non-Aspergillus invasive mould infections but clinical implementation is still very much limited by costs and technical and interpretative challenges.

Novel targets, such as urinary glycans and siderophores, show potential to diagnose invasive aspergillosis but are still investigational as well as host-based assays which hold promise to enhance diagnosis, risk stratification, disease monitoring and prognostication of invasive aspergillosis.