Title Modification of the Nomenclature of Procedures in Laboratory Medicine for the diagnostic laboratory procedures for *Aspergillus* diseases.

Agency HAS (French National Authority for Health - Haute Autorité de santé)
5 avenue du Stade de France – F 93218 La Plaine Cedex, France
Tel: +33 (0)1 55 93 70 00 – Fax: +33 (0)1 55 93 74 35, contact.seap@has-santé.fr, www.has-sante.fr

Reference ISBN number: 978-2-11-151483-6, link to full report in French: https://www.has-sante.fr/portail/jcms/c_2736666/fr/actualisation-des-actes-de-biologie-medicale-relatifs-au-diagnostic-des-infections-a-aspergillus

Aim

The aim of this work is to evaluate the accuracy of biological techniques for the diagnosis of *Aspergillus* (fungal diseases). It focuses on detection of fungal proteins (named soluble antigens) in blood or other biological fluids and on specific *Aspergillus* antibodies detection in serum.
This study was conducted with a view to inclusions or changes in the List of Procedures in Laboratory Medicine reimbursed by the National Health Insurance System in France.

Conclusions and results

The analysed data (from seventeen good practice guidelines, the point of views of six relevant professional bodies and of the National Reference Centre for Invasive fungal Infections and antifungal Medicines allow us to conclude that:

I - For the specific soluble antigens research

- This test is useful in case of suspicion of invasive aspergillosis as follows:
  - In a twice a week iterative screening for immunocompromised patients at high risk of invasive aspergillosis (at least 5%) in order to detect its occurrence early and provide therapeutic care if necessary;
  - As confirmatory test in addition to clinico-radiological examinations which led to this diagnosis ;
  - If positive, this test is useful in an iterative schedule after the initiation of an antifungal treatment to follow-up the response to this regimen.
- Two soluble antigens could be looked for: galactomannan (GM) or β-(1-3)-D-glucane (BG). In case of a clinico-radiological set of elements suggestive of aspergillosis, the search for GM is preferred. If the symptomatology is less precise, the BG is interesting because a negative result makes it possible to exclude an invasive fungal pathology;
- The sensitised latex technique must no longer be used (obsolete technique) for soluble antigens investigation. The techniques to be used are the immuno-enzymatic (ELISA) for GM and the colorimetric (modification of the Limulus Amebocyte Lysate pathway) assay for the BG;
- A confirmatory test of a soluble antigen positive result should be performed within 48 hours or at most 72 h, using the same technique on a second sample as applied for the initial test/assay and retesting the first one.

II - For the specific anti-*Aspergillus* antibodies (Ab) research in serum

- The search for specific Ab should be carried out by two different techniques: one for the initial inquiry and another method, when confirming the presence of an aspergillosis form;
- For the initial quest, the techniques for Ab search have to be standardised, reproducible, providing quantitative values (titration) for the Ab. These include the EIA;
- The current techniques for confirmation (COES, IELP or WB) are not commented on and are maintained.
- For the follow-up of patients by serum iterative assays (titration of Ab), the technique used should be able to quantitatively evaluate the kinetics of the Ab titles, starting from the initial detection.

Recommendations

Finally, taking into account the great variation of the results, HAS considers that the biological monitoring of an aspergillosis form by iterative tests (request of antigens or Ab) should be performed by the same technique and in the same medical laboratory in order to reduce the factors of variability.

Methods

The method consisted of:

- Performing a critical analysis of the identified summary literature (good practice guidelines, health technology assessment reports, general/systematic reviews and meta-analyses) after a systematic and

selective document search based on methodological quality;

- Then collecting the views of the professional health organisations concerned (Immunology and Allergology, Pneumology, Hematology, Infectious Biology, Transplantation and the National Reference Centre);
- These elements being summarised in an argument, submitted directly to the HAS Board for validation.

Written by

Véronique DAURAT, HAS (French National Authority for Health - Haute Autorité de santé), France.