ANCA testing and reporting in Switzerland: Recommendations of the Swiss Society for Allergology and Immunology (SSAI) - Commission on Laboratory Diagnostics (CLD)

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1. Individual laboratories must know and understand the performance characteristics and limitations of the assays they use.

2. When performing ANCA immunofluorescence (IIF) testing, both pattern and staining intensity (e.g., titer or fluorescence intensity (digital imaging system)) should be reported. It should be clear from the report that these results were obtained by immunofluorescence testing.

3. The reported ANCA pattern and staining intensity should be the result of testing on ethanol-fixed neutrophils. If other neutrophil substrates (for example, formalin-fixed neutrophils) are additionally used, the patterns observed on these substrates should not have an effect on the ANCA pattern reported to the clinician, which is the pattern obtained on ethanol-fixed neutrophils.

4. The reported ANCA pattern and staining intensity should be the result of immunofluorescence testing only. Results obtained by antigen-specific immunoassays should not have an effect on the reported immunofluorescence pattern.

5. A sample positive in ANCA IIF testing should be evaluated for the presence of anti-cellular antibodies (HEp-2 IIF). In case of positivity, the ANCA IIF report should indicate that -depending on the HEp-2 staining pattern and titer- ANCA IIF is not conclusive because of concomitant anti-cellular antibodies (e.g., ANA).

6. The ANCA nomenclature of the International Consensus Statement [1, 2] is recommended. Accordingly, the IIF pattern should be described as C-ANCA, C-ANCA (atypical), P-ANCA, or atypical ANCA. Other terms should not be used.

For detailed criteria of the ANCA IIF patterns we refer to the International Consensus Statement.

7. If IIF is used as a screening method to detect ANCA, any positive finding should be followed by both MPO- and PR3-specific immunoassays. *ANCA patterns do not reliably predict MPO- and/or PR3-specificity.*

A C-ANCA pattern correlates with PR3 specificity, but in some individuals may be due to MPO or other specificity. Likewise, a P-ANCA or atypical ANCA may be the result of MPO autoantibodies, but can also be due to antibodies with PR3 or other specificity.

8. If IIF is used as a screening method to detect ANCA, a positive result should not be reported to the clinician without the results of MPO- and PR3-specific immunoassays.

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A positive ANCA IIF result by itself is a nonspecific finding and may be misinterpreted by a health professional.

9. If MPO and PR3 antigen-specific immunoassays are used to screen for ANCA, any positive result should be followed by IIF testing or a second independent antigen-specific immunoassay [3]. Positive results of antigen-specific assays should not be reported to the clinician without having results of these confirmation tests available.

10. When reporting results of antigen-specific immunoassays for the detection of autoantibodies against MPO and PR3, the terms "MPO-ANCA" and "PR3-ANCA", respectively, should be used [4].

11. Results reported as MPO-ANCA and PR3-ANCA should have been obtained by an antigen-specific immunoassay only and not depend on IIF findings. When reported, MPO-ANCA and PR3-ANCA should not (additionally) contain the terms "P-ANCA" and/or "C-ANCA".

12. MPO-ANCA and PR3-ANCA should optimally be reported quantitatively, otherwise semi-quantitatively.

The likelihood ratio for small vessel vasculitis increases with antibody level, and reporting (semi)-quantitative data thus improves clinical interpretation.

13. MPO-ANCA and PR3-ANCA should not be reported in units containing the suffix I ("international").

None of the currently available commercial assays for the detection of MPO-ANCA and PR3-ANCA is standardized against an international certified reference material. The use of terms such as IU or UI/l falsely suggests that results obtained by different assays (laboratories) can be compared.

14. Any positive ANCA IIF and/or specific immunoassay test result in an unknown patient should be accompanied by a clear and concise interpretation of the ANCA results on the report.

ANCA test results are destined to be read by a variety of professionals involved in patient care, many of whom have little background in ANCA testing and are unable to fully interpret positive ANCA results.

15. The inclusion of an interpretation comment on positive ANCA results, and not just reporting the results themselves, is a responsibility of FAMH specialists in Clinical Immunology.

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Literature

1] Savige J, Gillis D, Benson E, et al. International Consensus Statement on Testing and Reporting of Antineutrophil Cytoplasmic Antibodies (ANCA). Am J Clin Pathol. 1999;111:507-513.

2] Savige J, Dimech W, Fritzler M, et al. Addendum to the International Consensus Statement on Testing and Reporting of Antineutrophil Cytoplasmic Antibodies. Am J Clin Pathol. 2003;120:312-318.

3] Bossuyt X, Cohen Tervaert JW, Arimura Y, et al. Position paper: Revised 2017 international consesnsus on testing of ANCAs in granulomatosis with polyangiitis and microscopic polyangiitis. Nat Rev Rheumatol. 2017;13:683-92.

4] Jennette J, Falk R, Bacon P, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum. 2012;65:1–11.

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