

# Upfront Screening of MPOPR3 Antibodies: A Change in our ANCA Testing Strategy

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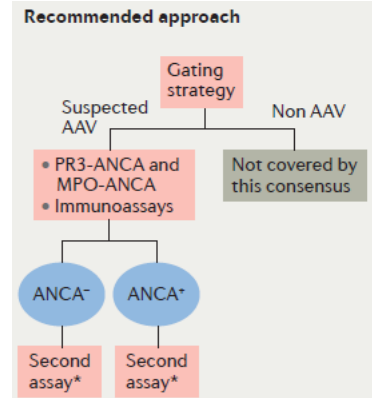
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## A Change in Consensus

In 2017, a revised international consensus on testing of ANCA in Granulomatosis with Polyangiitis (GPA) and Microscopic Polyangiitis (MPA) was published. Results from the multicentre European Vasculitis Study Group (EUVAS) showed large variability between different methods of IIF, yet good diagnostic performance of MPO/PR3 immunoassays, which had a higher specificity [1]. This led to the recommendation that screening with IIF followed by immunoassay testing was not necessary for maximal diagnostic accuracy in ANCA associated vasculitis.

The consensus recommends using high-quality antigen-specific assays for upfront screening, using a gating policy when requesting ANCAs that adheres to clinical guidelines and using a second immunoassay/and or IIF if both MPO and PR3 are negative but there is still strong clinical suspicion of small-vessel vasculitis [2].

**Key words:** Anti-neutrophil cytoplasmic Antibodies (**ANCA**), Indirect Immunofluorescence (**IIF**), Myeloperoxidase (**MPO**), Proteinase 3 (**PR3**), Granulomatosis with Polyangiitis (**GPA**), Microscopic Polyangiitis (**MPA**).



**Figure 1.** The revised 2017 recommendations for ANCA testing for patients suspected of having ANCA-associated vasculitis [2].

## Implementation

### Changes from our Current Method

Prior to the change, our ANCA testing strategy involved IIF on QUANTA Lyser 240 >interpretation by trained Biomedical Scientist> +ve samples have MPO/PR3 quantitation on BIO-FLASH.

In order to implement the new recommendations, we decided to:

1. Test all ANCA requests for MPO/PR3 on the BIO-FLASH as first line screening, everyday.
2. Test any NEW positive MPO/PR3 on IIF twice weekly. Known positives would get MPO/PR3 testing only.

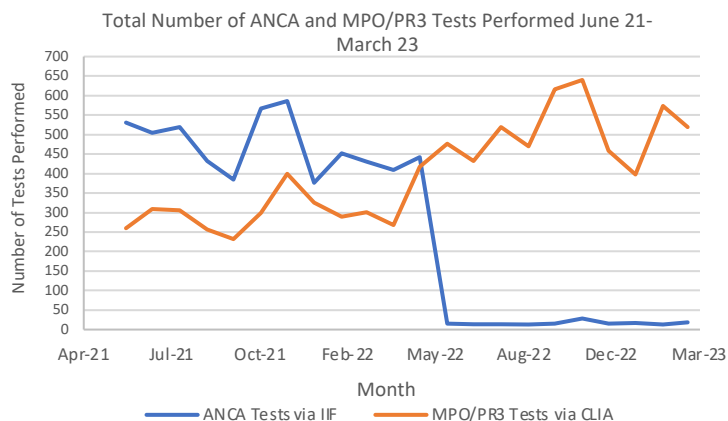
### Flow of Work

Changes made in the lab:

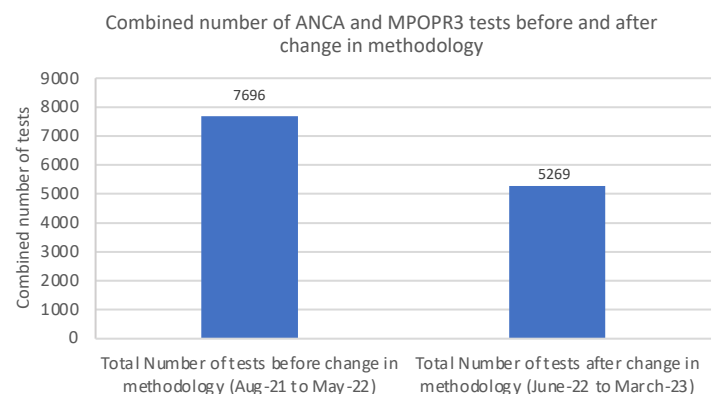
- Less time needed for the running the QUANTA Lyser 240 and for interpretation of IIF slides.
- BIO-FLASH workload increased, leading to a supportive MLA role.
- MPO/PR3 worklist created 3x per day.
- Any new positive MPO/PR3s would be tested via IIF on Tuesdays and Thursdays.

### Gating Strategy and IT Changes

- Gating strategies were trialed in the lab but it was not possible due to various difficulties.
- We set up gating on electronic requests from ICE and Medway which includes GPs and inpatient requests.
- The requesting terminology asked requesting clinicians to verify they are suspecting ANCA Vasculitis.
- The Biomedical Scientist reporting results flagged new positives to an Immunology medic for appropriate clinical interpretation.



**Figure 2.** Total number of MPO/PR3 tests (via CLIA) and ANCA test (via IIF) performed from June 2021- March 2023. Go live for MPO/PR3 upfront testing was May 2022. Following this, the number of ANCA IIF tests drastically decreased. MPO/PR3 via CLIA increased steadily.



**Figure 3.** When comparing the combined number of ANCA and MPO/PR3 tests 10 months before and after the change in methodology, there is a total decrease of 2427 tests after the change.

## What does this Change Mean for Patients?

ANCA screening is a common diagnostic tool to test for AAV [2]. This change means there is a reliable antigen-specific immunoassay being used to screen with an improved diagnostic performance.

The gating for the electronic requests will reduce the amount of ANCA test requests in some instances and improves the diagnostic testing performance with the reduction in false positives.

## New Outcomes and Learning

Although we are only in the early stages of the new ANCA testing strategy we can see it has been a positive change. The use of an automated platform for screening will reduce the manual resource needed to perform this assay and the variability seen using IIF as a screening tool.

## REFERENCES:

- [1] Damoiseaux, J. et al. Detection of antineutrophil cytoplasmic antibodies (ANCAs): a multicentre European Vasculitis Study Group (EUVAS) evaluation of the value of indirect immunofluorescence (IIF) versus antigen-specific immunoassays. *Ann. Rheum. Dis.* 76, 647–653 (2017)
- [2] Bossuyt, X., Cohen Tervaert, JW., Arimura, Y. et al. Revised 2017 international consensus on testing of ANCAs in granulomatosis with polyangiitis and microscopic polyangiitis. *Nat Rev Rheumatol* 13, 683–692 (2017).