ANTI NEUTROPHIL CYTOPLASMIC ANTIBODY (ANCA) TESTING GUIDELINES

Version:	1.0
Ratified by:	Clinical Biochemistry Senior Staff Group
Date ratified:	
Name of originator/author:	Dr Joanna Sheldon / Dr Tim Doulton/Lorna Miller
Director responsible for implementation:	Dr Edmund Lamb
Date issued:	March 2018
Review date:	March 2021
Target audience:	Clinical staff (medical, nursing and scientific), Trust wide and primary care

Version Control Schedule

Version	Date	Author	Status	Comment
1.0	10th January 2018	Mrs Lorna Miller	Active	

Contents

1 Policy Summary

This policy gives guidance on when to request ANCA.

2 Introduction

Anti-neutrophil cytoplasmic antibodies (ANCA), such as those directed towards proteinase-3 (PR3) and myeloperoxidase (MPO), are associated with a sub-type of small vessel vasculitis known as ANCA-associated vasculitis (AAV), a term that comprises granulomatosis with polyangiitis (GPA, formerly known as Wegener's granulomatosis) and microscopic polyangiitis (MPA). Screening for the presence of ANCA is a commonly used diagnostic test for AAV.

In this brief guideline, we outline the inherent limitations of ANCA for this purpose, and draw requestor's attention to guidance around requesting and interpretation of ANCA.

2.1 Requesting and interpretation of ANCA tests

Pre-test probability is defined as the probability of a condition being present BEFORE a diagnostic test is performed. As a patient goes through a diagnostic process, their signs and symptoms help to guide the test requesting and should improve the pre-test probability for each test.

In a completely unselected group of subjects, the overall incidence for ANCA associated vasculitis is approx. 15 cases/million in the UK. In an unselected "patient" population, the pre-test probability is too low to make ANCA testing useful as a screening test.

Only when a patient has clinical features of ANCA associated vasculitis does the pre-test probability approach a level where ANCA testing is likely to be useful.

The value of a diagnostic test is also related to the clinical specificity (negativity in health) and sensitivity (positivity in disease) of that test. ANCA testing can show both poor specificity and poor sensitivity (see below) and this, combined with a low pre-test probability, makes it vital that ANCA testing is requested very carefully in those with clinical evidence of disease.

2.2 ANCA detection methods

There are many different methods for detection and quantification of ANCA and the specific antibodies to MPO and PR3. There is no perfect method and every method shows some false positive results; this can be up to 10% of samples from patients who do NOT have ANCA associated symptoms [1]. Similarly every method shows false negative results which can be between 10-30% of samples. This means that up to 30% of newly presenting patients with an

eventual confirmed diagnosis of AAV will have a negative ANCA result by one or more of the methods currently in use - indirect immunofluorescence (IIF, the EKHUFT standard screening test) or by immunoassay (usually ELISA, the EKHUFT standard confirmatory test).

It is therefore essential that requestors understand that ANCA should only be requested and interpreted in the correct clinical context.

3 Purpose and Scope

This policy gives guidance that is consistent with published international consensus papers.

4 Definitions

ANCA - Anti-neutrophil cytoplasmic antibodies
MPO - myeloperoxidase
PR3 – proteinase-3
AAV - ANCA-associated vasculitis
GPA - granulomatosis with polyangiitis
MPA - microscopic polyangiitis
IIF – indirect immunofluorescence
ELISA – enzyme linked immunosorbant assay
eGFR – estimated glomerular filtration rate
CRP – C reactive protein

5 Duties

All staff involved in requesting ANCA must adhere to this policy.

6 Policy specific information

6.1 Requesting ANCA

ANCA should be requested ONLY in patients with the following present symptoms/symptom complexes [2]:

- Urinary findings suggestive of glomerulonephritis (e.g. blood +/- protein on urine dipstick) with or without co-existent declining eGFR
- Pulmonary haemorrhage or pulmonary-renal syndrome
- Cutaneous vasculitis with systemic features

- Multiple lung nodules or other radiological evidence typical of AAV
- Asthma with eosinophilia or other systemic features *
- Chronic destructive disease of the upper airways
- Long-standing sinusitis or otitis
- Subglottic tracheal stenosis
- Mononeuritis multiplex or other peripheral polyneuropathy
- Retro-orbital mass
- Scleritis
- Altered cognitive function with systemic features *
- Otherwise unexplained systemic disease *

(* Typically would include, but not limited to, any of: unintentional weight loss, pyrexial >38℃, fevers, sweats, myalgia, arthralgia, raised CRP in absence of infection)

6.2 Interpretation of ANCA

- A single immunoassay will be at best 90% sensitive. Where a high clinical suspicion exists and immunoassay results are negative, the immunology laboratory will, upon request, use an alternative immunoassay method.
- Where clinical suspicion remains high following negative immunoassay results by two different assay methods it is recommended to undertake biopsy of an affected organ.
- Other conditions may result in false positive ANCA testing either by IIF or immunoassay methods. For example, in two series of patients with infective endocarditis, ANCA positivity was found in around 20% of patients. Therefore, clinical features of diseases that are commonly associated with ANCA positivity and/or may mimic AAV clinically (infection endocarditis, tuberculosis, inflammatory bowel disease, hepatitis B & C, malignancy) should be sought and excluded using appropriate alternative investigations where necessary.
- The presence of anti-nuclear antibodies may result in false positive perinuclear ANCA staining pattern by IIF.

Contact details for queries and advice

Lorna Miller, Clinical Scientist, Immunology Laboratory, William Harvey Hospital

01233 616716

lornamiller1@nhs.net

Dr Joanna Sheldon, St George's Protein Reference Unit

0208 725 5752

jsheldon@sgul.ac.uk

7 Key Stakeholders, Consultation, Approval and Ratification Process

East Kent Hospitals University NHS Foundation Trust is the key stakeholder for this policy. This document was prepared in consultation with renal, rheumatology and neurology consultants.

8 Review and Revision Arrangements

Three years from implementation date, by author.

9 Dissemination and Implementation

Trustnet, by proactive implementation through the Divisions by appropriate clinical leads and by proactive dissemination to primary care partners and other Kent Trusts using the EKHUFT Immunology laboratory service. A link to these guidelines will be added to ANCA reports.

10 Document Control including Archiving Arrangements

Archive of this document will be through Q Pulse with the current version held on Trustnet.

11 Monitoring Compliance

Within the Trust, compliance with this policy must rest with the requesting Divisions. Compliance will be assessed by retrospective audit.

12 References

1 - Csernok E. & Moosig F Current and emerging techniques for ANCA detection in vasculitis. Nat. Rev. Rheumatol 2014;10: 494–501)

2 – Bossuyt et al. Revised 2017 international consensus on testing of ANCA in granulomatosis with polyangiitis and microscopic polyangiitis Nat Rev Rheum 2017

13 Associated Documentation

Not applicable

Appendix A - Equality Impact Assessment

Equality and Human Rights Impact Analysis (EHRIA)

Part One – Screening Tool

Name of the policy, strategy, function or methodology:	ANCA testing guidelines

Details of person completing the EHRIA	
Name	Mrs Lorna Miller
Job Title	Clinical Scientist
Directorate/Department	CSSD/Immunology
Telephone Number	723 6176

1. Identify the policy, strategy, function or methodology aims

What are the main aims, purpose and outcomes of the policy, strategy, function or methodology?
To outline the inherent limitations of ANCA, and draw requestor's attention to guidance around requesting and interpretation of ANCA.
Does it relate to our role as a service provider and/or an employer?
Service provider.

2. Assess the likely impact on human rights and equality

Use this table to check if the policy, strategy, function or methodology:

- could have a negative impact on human rights or on any of the equality groups, or
- could have a positive impact on human rights, contribute to promoting equality, equal opportunities or improve relations.

It is not necessary to complete each box, nor to mark whether it is positive or negative, although you can do this if you find it helpful.

	Protected Characteristic								
	Race	**Sex**	**Disability**	**Sexual Orientation**	**Religion or belief**	**Age**	**Gender reassignment**	**Marriage & Civil Partnership**	**Pregnancy & Maternity**
Could this policy, procedure, project or service affect this group differently from others? **YES/NO**									
Could this policy, procedure, project or service promote equal opportunities for this group? **YES/NO**									
Right to life *e.g. decisions about life-saving treatment, deaths through negligence in hospital*									
Right not to be tortured or treated in an inhuman or degrading way									
Right to respect for private and family life e.g. *respecting lgb relationships, confidentiality*									
Right to freedom of thought, conscience and religion *e.g. respect for cultural and religious requirements*									
Right to freedom of expression *e.g. access to appropriate communication aids*									
Right to freedom of assembly and association *e.g., right to representation, to socialise in care settings*									
Right to education *e.g. access to basic knowledge of hygiene and sanitation*									
Right to liberty e.g. informal detention of patients who do not have capacity									

3. How does it impact on people's human rights and equality?

Using the table above, explain anticipated impacts. If a full EHRIA is recommended, you can summarise the impacts - it is not necessary to set these out in detail,

Could people's human rights be impacted negatively? Could the policy, strategy, function or methodology result in inequality or discrimination?
No
Could this policy, strategy, function or methodology result in positive impacts on people's human rights or equality? Could it present opportunities to promote equality?
No

4. Recommendations

Is a full EHRIA recommended? If not, give reasons
No. The policy has equal impact.

5. Publication of EHRIA

Give details of where Screening Tool or the full EHRIA will be published and when this will take place
n/a.

Details of person completing the EHRIA	
Name	Mrs Lorna Miller

Signed

Date:

Approval and sign-off	Name
Head of Department/Director	Mr Edward Kearney

Signed …… Date: ……

Appendix B – Author's Checklist of compliance with the Policy for the Development and Management of Organisation Wide Policies and Other Procedural Documents

POLICY:

To be completed and attached to any policy when submitted to the appropriate committee for consideration and approval.

	Requirement:	Compliant Yes/No/ Unsure	Comments
1.	**Style and format**	Yes	
2.	**An explanation of any terms used in documents developed**	Yes	
3.	**Consultation process**	Yes	
4.	**Ratification process**	Yes	
5.	**Review arrangements**	Yes	
6.	**Control of documents, including archiving arrangements**	Yes	
7.	**Associated documents**	n/a	
8.	**Supporting references**	Yes	
9.	**Relevant NHSLA criterion specific requirements**	n/a	
10.	**Any other requirements of external bodies**	n/a	
11.	**The process for monitoring compliance with NHSLA and any other external and/or internal requirements**	n/a	

Appendix C – Plan for Dissemination of Policies

To be completed and attached to any policy when submitted to the appropriate committee for consideration and approval.

Title of document:	ANCA TESTING GUIDLEINES		
Version Number:	1.0		
Approval Date:		**Dissemination lead:**	
Previous document already being used?	Yes		
If yes, in what format (paper / electronic) and where (e.g. Directorate / Trust wide)?	Electronic on Q-Pulse and Trustnet		
Proposed instructions regarding previous document:			

To be disseminated to:	**How will it be disseminated, who will do it and when?**	**Format (i.e. paper or electronic)**	**Comments:**
Trust clinical staff	Trustnet	electronic	
Trust clinical staff	Newsletters	electronic	

Author's Dissemination Record - to be Used Once Document is Approved – to be kept with the master document

Date document forwarded to be put on the Trust's central register / in SharePoint:		**Date document put on Directorate register (if appropriate) / on Directorate webpage (if applicable)**	

Disseminated to: (either directly or via meetings, etc.)	**By Whom?**	**Format (i.e. paper or electronic)**	**Date Disseminated:**