DIABETES AUTOANTIBODY REQUESTING GUIDELINES

Version:	1.0
Ratified by:	Clinical Biochemistry Senior Staff Group
Date ratified:	18.5.2017
Name of originator/author:	Dr Joanna Sheldon / Lorna Miller
Director responsible for implementation:	Dr Edmund Lamb
Date issued:	6.6.2017
Review date:	June 2019
Target audience:	Clinical staff (medical, nursing and scientific), Trust wide and primary care

Version Control Schedule

Version	Date	Author	Status	Comment
1.0	6th June 2017	Mrs Lorna Miller	Active	

Contents

1 Policy Summary

This policy gives guidance on when to request diabetes autoantibodies.

2 Introduction

Type I diabetes represents between 10 and 15% of all diabetes. Approximately 70% of the beta- cells in the islets of Langerhans make insulin with the other cells making glucagon, somatostatin and pancreatic polypeptide. At the diagnosis of type I diabetes, the histology of the islets show a mixture of patterns. Early in the disease process, the islets will appear normal with few infiltrating cells. Gradually the intact beta-cells become surrounded by activated T and B lymphocytes and antigen presenting cells and finally the beta cells will be destroyed and the tissue shows no inflammatory cells. The pathogenic process is T cell driven but during the cellular destruction, antigens are released and the immune system can make autoantibodies to these previously "hidden" antigens and to insulin. Antibodies to these antigens are summarised in Table 1; they are not pathogenic and are only seen "associated" with type I diabetes rather that cause type I diabetes and this limits their diagnostic utility.

Table 1 – the antigens associated with autoantibodies in Type I diabetes.

Antigen/ autoantibody	Islet specificity	Function	% of patients positive at diagnosis
Glutamic Acid Decarboxylase (GAD)	No – present in other islet cells and CNS	Catalyses synthesis of ɣ amino butyric acid (neurotransmitter) – likely regulates insulin release	65 -75%, more in adults - (also a target in stiff person syndrome)
Islet Tyrosine Phosphatase (IA-2)	No – present in other islet cells and CNS	Unknown	50-60%, more in children
Zinc transporter 8 (ZnT8)	β cell specific	Zinc transport	50-60%

Diagnosis of Type 1 Diabetes

Diagnosis of type I diabetes is based on the WHO criteria and includes the concentrations of blood glucose and HbA1c. Neither the presence of autoantibodies nor the concentration of the autoantibodies is part of the diagnostic criteria.

The role of autoantibodies in the investigation and management of patients with diabetes

The measurement of these antibodies in patients with diabetes is part of many research projects and it is clear that the presence of these antibodies does confer an increased risk

of developing type I diabetes. Positivity of at least 2 of the autoantibodies (GAD, IA-2, ZnT8) gives a patient a 10% per year risk of developing type I diabetes and over a 20 year period, the majority of these patients (>95%) will have developed type I diabetes.

Patients with atypical presentations e.g. adults thought to be type 2 diabetics but with increasing insulin requirements (LADA) may benefit from antibody testing to better classify their diabetes. The prevalence of all 3 autoantibodies is < 1% in MODY and testing for these close to diagnosis can be used to discriminate type 1 diabetes from MODY.

Analytical and technical considerations

There is no certified reference preparation or EQA programme for antibodies to any of the antigens associated with type 1 diabetes.

The timing of samples with respect to the time of diagnosis of type I diabetes is important. There is a narrow and variable window of antibody positivity around the time of diagnosis and the false negative rate increases as the time from diagnosis increases.

When should the antibodies be used?

- Diabetes autoantibodies should not be measured routinely to confirm type 1 diabetes in adults, children or young people (NICE CG 17 and 18)
- Consider measurement of diabetes autoantibodies in adults if classification is uncertain and confirming type 1 diabetes would have implications for therapy (NICE CG17)
- Consider measurement of diabetes autoantibodies in adults if type 1 diabetes is suspected, but the clinical presentation is atypical (NICE CG17)
- Autoantibody tests have their lowest false negative rate at the time of diagnosis, and the false negative rate rises thereafter (NICE CG 17)

What autoantibodies should be requested?

- If diabetes autoantibodies are measured, 2 different diabetes specific antibodies should be done to reduce the false negative rate (NICE CG17).
- Samples will be sent to the Royal Devon and Exeter laboratory for their panel of 3 autoantibodies (GAD, IA-2 and ZnT8). Islet cell antibody will no longer be available.

3 Purpose and Scope

This policy gives guidance that is consistent with guidance developed by NICE (NG17 and 18)

4 Definitions

GAD - Glutamic Acid Decarboxylase antibody

IA-2 – islet antigen 2 antibody

ZnT8 – zinc transporter 8 antibody

LADA – latent autoimmune diabetes in adults

MODY – maturity onset diabetes of the young

5 Duties

All staff involved in requesting diabetes autoantibodies must adhere to this policy.

6 Policy specific information

Diabetes/endocrine Consultant request only

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 diabetes and endocrine consultants and clinical commissioning groups.

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.

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

Diabetes (type 1 and type 2) in children and young people: diagnosis and management
NICE guideline (NG18): August 2015
https://www.nice.org.uk/guidance/ng18

Type 1 diabetes in adults: diagnosis and management
NICE guideline (NG17): August 2015
https://www.nice.org.uk/guidance/ng18

Bingley P 2010 Clinical applications of diabetes antibody testing. J Clin Endocrinol Metab 95(1):25-53

Brooking H, Ananieva-Jordanova R, Arnold C, Amoroso M, Powell M, Betterle C, Zanchetta R, Furmaniak J, Smith BR. A sensitive non-isotopic assay for GAD65 autoantibodies. Clin Chim Acta. 2003 May; 331(1-2):55-9.

Nilson E, Ekholm B, Rees Smith B, Törn C, Hillman M. Calcium addition to EDTA plasma eliminates falsely positive results in the RSR GADAb ELISA. Clin Chim Acta. 2008 Feb; 388(1-2):130-4.

A comparison of serum and EDTA plasma in the measurement of glutamic acid decarboxylase autoantibodies (GADA) and autoantibodies to islet antigen-2 (IA-2A) using the RSR radioimmunoassay (RIA) and enzyme linked immunosorbent assay (ELISA) kits. Rahmati K, Lernmark A, Becker C, Foltyn-Zadura A, Larsson K, Ivarsson SA, Törn C. Clin Lab. 2008; 54(7-8):227-35.

McDonald TJ, Colclough K, Brown R, Shields B, Shepherd M, Bingley P, Williams A, Hattersley AT, Ellard S. 2011. Islet autoantibodies can discriminate maturity-onset diabetes of the young (MODY) from Type 1 diabetes. Diabet Med 28:1028-1033.

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:	Diabetes autoantibody requesting 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 ensure a consistent and rational approach to the requesting of diabetes autoantibodies
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:	DIABETES AUTOANTIBODY REQUESTING 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:**