Glutamic Acid Decarboxylase Antibodies

General information

Antibodies against the 65 isoform of the enzyme glutamic acid decarboxylase (GAD65) are seen in around 80% of patients with Type 1 Diabetes Mellitus (T1DM) (Dade et al, 2020). However they are also associated with neurological disorders. The most common of these is Stiff Person Syndrome but they have also been implicated in some cases of temporal lobe epilepsy, cerebral ataxia and limbic encephalitis, as well as overlap syndromes (Dade et al, 2020).

GAD antibodies can be ordered individually, or as part of an autoimmune diabetes panel containing IA-2 antibodies, ZnT8 antibodies and GAD antibodies.

Assay Interferences: Lipaemic or haemolysed samples should not be used.

Laboratory information

Analyte: Glutamic Acid Decarboxylase (GAD) Antibodies

Units: U/mL

Specimen type: Serum (Brown top serum gel bottle)

Frequency of analysis:

For autoimmune diabetes: At initial diagnosis and in patients with suspected type 1 diabetes. Highest accuracy seen at initial presentation.

For Stiff person syndrome: At initial diagnosis and at significant change of clinical symptoms

Turnaround times: Median – 6

Specimen transport: At room temperature

Additional/Special requirements: None

Method: ELISA

Participation in EQA scheme: UK NEQAS for Diabetic Markers

Clinical information

Interpretation: Autoimmune diabetes associated autoantibodies (ADAA) can be seen before clinical symptoms and used to stratify risk of progression to overt diabetes. In patients without a current diabetes diagnosis the likelihood of progression to diabetes within 5 years increases as additional antibody positivity increases. The 5-year risk of progression with only Islet cell antibody positivity is 2.2% but this increases up to 70% when 3 additional antibodies (including ZnT8, IA-2 and GAD65) are also present (Polly, 2010). ADAA positivity can be lost as islet cell destruction progresses leading to misleading negative results. NG17 states the false negative rate can be reduced by carrying out quantitative tests for 2 different diabetes specific autoantibodies (with at least 1 being positive). Serum C-peptide should be used if there is still diagnostic uncertainty after the use of autoantibody testing.

GAD65 antibody levels are commonly much higher in serum in neurological syndromes than in T1DM, and higher in CSF in cerebella ataxia and limbic encephalitis than in stiff person syndrome (Budhram et al, 2021)

Reference Range: Negative is <5 U/mL

Budhram, A., Sechi, E., Flanagan, E. P., Dubey, D., Zekeridou, A., Shah, S. S., Gadoth, A., Naddaf, E., McKeon, A., Pittock, S. J. & Zalewski, N. L. (2021). Clinical spectrum of high-titre GAD65 antibodies. *Journal of neurology, neurosurgery, and psychiatry*, *92*(6), 645–654.

Dade, M., Berzero, G., Izquierdo, C., Giry, M., Benazra, M., Delattre, J. Y., Psimaras, D., & Alentorn, A. (2020). Neurological Syndromes Associated with Anti-GAD Antibodies. *International journal of molecular sciences*, *21*(10),

Polly J. Bingley (2010) Clinical Applications of Diabetes Antibody Testing, *The Journal of Clinical Endocrinology & Metabolism*, **95**, 25–33

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