

## Coxsackievirus and Diabetes mellitus:

An overlooked important connection

### NAISSA NEWS

NAISSA - Enzyme immunoassay for qualitative detection of Coxsackievirus B lgM/lgG (Ref. N145D24CXM, N146D24CXG)

#### General information

**Diabetes mellitus type 1** also called the insulin-dependent diabetes mellitus is a chronic autoimmune disease induced by the destruction of insulin-producing b-cells of Langerhans' islets caused by autoimmune inflammation reaction. This is characterized by a large or complete lack of insulin production. Diabetes mellitus type 1 represents 5–10% of all cases of diabetes, a disease with frequently serious and severe consequences for the patient such as ketosis, ketoacidosis, microangiopathy, cerebral vascular accidents, retinopathies, cataract, glaucoma, hypertension, ischaemic cardiomyopathy, glomerulosclerosis and gangrene [1].

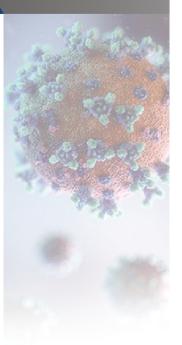
**Enteroviruses** are considered the main viral candidates for causing type 1 diabetes in humans [2]. A recent systematic review that analyzed papers published on this topic documented a significant association between enteroviruses and autoimmunity/type 1 diabetes [3].

**Coxsackie B virus (CVB)** is the most prevalent enterovirus in pre-diabetic and diabetic patients [2]. Several studies have reported the presence of CVB RNA in the blood of type 1 diabetes patients [4–7]. There is even evidence of CVB4 being detected in pancreatic tissue from patients with type 1 diabetes [8]. The molecular basis of autoimmunity in CVB4 infection is proposed to be a **molecular mimicry** [9], where the 2C non-structural CVB protein has a shared sequence with the glutamic acid decarboxylase 65 enzyme (GAD65), which is predominantly expressed in pancreatic beta cells [10]. This results in immunological cross-reactivity caused by sequence similarity between self- and non-self-antigens. Particularly GAD65 was found to play an important role in the pathogenesis of type I diabetes as a target autoantigen [11]. **Bystander activation** of autoreactive T cells and rapid death of CVB-infected beta cells was also a suggested mechanism by which CVB4 induces and accelerates diabetes.

NAISSA is the only platform that provides fully automated detection of IgM and IgG antibodies to Coxsackie B virus.

#### **Diagnostic Efficiency**

Product	Sensitivity	Specificity
Coxsackievirus B IgM	>98%	>98%
Coxsackievirus B IgG	>98%	>98%





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**NAISSA also enables the detection of antibodies against insulin** (present in up to 70% of patients), with these autoantibodies being a marker for destruction of insulin producing b-cells. Anti-insulin antibodies are found in 37% of patients with newly detected diabetes type I and in 2-6% of their relatives of the first degree.

#### REFERENCES

1. Jaïdane, H.; Hober, D. Role of coxsackievirus B4 in the pathogenesis of type 1 diabetes. Diabetes & Metabolism 2008, 34, 537–548

2. Filippi, C.M.; von Herrath, M.G. Viral trigger for type 1 diabetes: Pros and cons. Diabetes 2008, 57, 2863–2871 3. Smatti, M.K.; Cyprian, F.S.; Nasrallah, G.K.; Al Thani, A.A.; Almishal, R.O.; Yassine, H.M. Viruses and Autoimmunity: A Review on the Potential Interaction and Molecular Mechanisms. Viruses 2019, 11, 762. https://doi.org/10.3390/v11080762

Clements, G.; Galbraith, D.; Taylor, K. Coxsackie B virus infection and onset of childhood diabetes. Lancet 1995, 346, 221–223.
Andréoletti, L.; Hober, D.; Hober-Vandenberghe, C.; Belaich, S.; Vantyghem, M.-C.; Lefebvre, J.; Wattré, P.; Hober-Vandenberghe, C.; Vantyghem, M. Detection of Coxsackie B Virus RNA sequences in whole blood samples from adult patients at the onset of type I diabetes mellitus. J. Med. Virol. 1997, 52, 121–127.

6. Andréoletti, L.; Hober, D.; Hober-Vandenberghe, C.; Fajardy, I.; Belaich, S.; Lambert, V.; Vantyghem, M.C.; Lefebvre, J.; Wattre, P. Coxsackie B virus infection and beta cell autoantibodies in newly diagnosed IDDM adult patients. Clin. Diagn. Virol. 1998, 9, 125–133.

7. Oikarinen, S.; Martiskainen, M.; Tauriainen, S.; Huhtala, H.; Ilonen, J.; Veijola, R.; Simell, O.; Knip, M.; Hyöty, H. Enterovirus RNA in blood is linked to the development of type 1 diabetes. Diabetes 2011, 60, 276–279.

8. Dotta, F.; Censini, S.; van Halteren, A.G.; Marselli, L.; Masini, M.; Dionisi, S.; Mosca, F.; Boggi, U.; Muda, A.O.; Del Prato, S.; et al. Coxsackie B4 virus infection of beta cells and natural killer cell insulitis in recent-onset type 1 diabetic patients. Proc. Natl. Acad. Sci. USA 2007, 104, 5115–5120.

9. Kaufman, D.L.; Erlander, M.G.; Clare-Salzler, M.; Atkinson, M.A.; MacLaren, N.K.; Tobin, A.J. Autoimmunity to two forms of glutamate decarboxylase in insulin-dependent diabetes mellitus. J. Clin. Investig. 1992, 89, 283–292.

10. Hou, J.; Said, C.; Franchi, D.; Dockstader, P.; Chatterjee, N.K. Antibodies to Glutamic Acid Decarboxylase and P2-C Peptides in Sera from Coxsackie Virus B4-Infected Mice and IDDM Patients. Diabetes 1994, 43, 1260–1266.

11. Yokota, I.; Shima, K. GAD antibody in IDDM. Rinsho. Byori. 1998, 46, 331–337.

Product	Order No.	Kit
Coxsackievirus B IgM	N145D24CXM	24 tests
Coxsackievirus B lgG	N146D24CXG	24 tests
Anti Insulin	N281A24INS	24 tests

### NAISSA monotest immunoanalyzer - BENEFITS

- ✓ One Cartridge one test
- Simplify operation just add sample and click RUN
- Save your time ready to use reagents
- ✓ Factory precalibrated
- ✓ QC material included
- ✓ No crossover Cartridge laminated with three layers plastic foil, provide completely safety and stability
- Quantitative evaluation of results
- ✓ High diagnostics specificity and sensitivity
- ✓ High reproducibility
- ✓ Total automatisation
- Small package size (24 tests, calibrators and control)



