*Workshop report***Immunology and Diabetes Workshops: Report of the Second International Workshop on the Standardisation of Cytoplasmic Islet Cell Antibodies**

Summary of a Workshop organised by the Immunology and Diabetes Workshops Committee, supported in part by the Juvenile Diabetes Foundation International, and held at the "Science at Sea - 1987" meeting in Perth, Western Australia, from 20-22 January 1987

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The clinical onset of Type 1 (insulin-dependent) diabetes mellitus is associated with a high prevalence of islet cell (cytoplasmic) antibodies (ICA). Determination of ICA is increasingly used in various clinical investigations to identify individuals at risk for Type 1 diabetes, to classify the diabetic syndrome, and to monitor diabetic patients undergoing either immunomodulating therapy or islet and segmental pancreas transplantation.

It has been suggested that the presence of ICA is a marker of autoimmune destruction of the pancreatic B cells, and that the ICA test may be of predictive value for the development of Type 1 diabetes. Standardisation of the ICA assay is therefore obligatory to permit inter-laboratory comparison. The precision and reproducibility of the ICA test has not been defined. It has thus not been possible to compare ICA results reported from different laboratories.

The results of the First International Workshop on ICA Standardisation indicated that the availability of reference sera would allow standard curves to be established and used to define ICA in arbitrary units [1]. The First Workshop did not, however, address a test for precision and reproducibility. For this reason a Stage 2 trial on ICA standardisation was carried out. The results were presented and discussed during the Second Workshop held at the recent conference "Science at Sea - 1987" in Perth, Western Australia.

Well ahead of this conference a series of 22 coded 0.5 ml freeze-dried serum samples were prepared and distributed. The set of coded samples included a reference standard representing serum from a 12-year-old child with newly diagnosed Type 1 diabetes. The reference standard was diluted 1:2, 1:4, 1:8 and 1:16 in pooled ICA-negative normal human serum. In addition, there were 4 serum samples from healthy individuals and 10 serum samples from 8- to 16-year-old newly diagnosed Type 1 patients. The reference standard samples were included in duplicates in order to test for assay precision.

In order to determine intralaboratory assay reproducibility over a period of time, each laboratory first received one set of samples, to be followed by a re-coded second set upon submission of the results of end-point titres of the first set of samples. The two sets of 22 serum samples were received 3-8 months apart. A total of 35 international laboratories submitted their results to the Workshop.

At the time of the conference, results for both sets of reference standards were available from 26 laboratories. All these laboratories used the indirect immunofluorescence technique for ICA. A broad range of titres were reported. The lower detection limit covered the complete range of the standard sera dilutions, as did the duplicate estimations within some laboratories. Hence, some laboratories were unable to measure ICA in the concentration range of the standards, while others could reproduce detection of ICA throughout this range.

Arbitrary units (JDF units) relative to the degree of dilution were assigned to the standard sera. The end-point titres of the additional 12 coded samples were then compared for each participating laboratory which could produce a standard curve. Retrospective conversion of ICA titres into "JDF units" appeared to improve precision within the laboratories. In addition, there was an improvement in concordance between laboratories. It was therefore concluded that the introduction of a reference standard to generate a standard curve for each assay is a useful approach to improve precision and reproducibility of ICA determination within and between laboratories.

Based on the presented data, the Immunology and Diabetes Workshops Committee recommended that the current reference standard be made available to interested investigators to establish their own ICA reference standard. It was also recommended that investigators who are able to obtain a standard curve with this reference standard are encouraged to participate in a Stage 3 workshop. The purpose of the Stage 3 analysis is to determine whether the precision and inter-laboratory concordance can be further improved by laboratories measuring ICA levels in "JDF-units" rather than end-point titres. This approach might make it possible to define predictive values for ICA and allow an assessment of geographical, population and methodological differences.

Laboratories interested in participating in the Stage 3 workshop on ICA standards are kindly asked to request the current reference standard and Workshop sera from Dr. Helga Gleichman, Immunology and Diabetes Workshops (IDW) Secretariat, Diabetes-Forschungsinstitut, Auf'm Hennekamp 65, D-4000 Düsseldorf 1, FRG. It is anticipated that each participant will be able to submit results on a total of 50 coded samples before the end of June 1987. It is planned that the results of the Stage 3 serum exchange be discussed at the Third International Workshop on the standardisation of cytoplasmic islet cell antibodies in an IDW conference, again supported by the Juvenile Diabetes Foundation International, to be held in New York on October 24-25, 1987.

References

1. Bottazzo GF, Gleichmann H (1986) Immunology and Diabetes Workshops: report of the first international workshop on standardisation of cytoplasmic islet cell antibodies. *Diabetologia* 29: 125-126

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