FINAL REPORT

Working Party on Standardization of the factor VIII:C assay

The Working Party for the standardization of the factor VIII:C assay was set up in 1977 following the Oxford Workshop on the factor VIII assay held in November, 1976. The first meeting of the Working Party was held at the NIBSC on December 21st, 1977 with the following members:-

Dr. C.R. Rizza (Chairman)
Dr. T.W. Barrowcliffe (NIBSC)
Prof. G.I.C. Ingram (St. Thomas')
Mr. T.B.L. Kirkwood (NIBSC) (Secretary)
Mr. I.L. Rhymes (Oxford)

Subsequent to the first meeting:

Dr. I.R. Peake (Cardiff)
Dr. M. Seghatchian (Edgware BTC)
Mr. T.J. Snape (PFL, Oxford)

were asked to join the Working Party.

Dr. E.G.D. Tuddenham (Royal Free) and Mr. A. .D. Curtis (NIBSC) respectively took the place of Professor Ingram, after his retirement & of Mr. Kirkwood when he moved from NIBSC to Mill Hill.

The overall aim of the Working Party was to improve comparability of results of factor VIII:C assays in laboratories throughout Britain with particular reference to:

1. Identification and standardization of individual reagents which might be the source of discrepancy in the assay system.
2. Study of the causes of discrepancy between 1-stage and 2-stage assays of concentrates.
3. Improvement of comparability of standards used in the assays.

As a preliminary to the above points of investigation, a questionnaire was sent to all Haemophilia Centres, Blood Transfusion Centres and Fractionation Laboratories to ascertain details of reagents, assay methods and standards in use at the time. The

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results of this survey were published in Clinical and Laboratory Haematology (1981, 3, 186-189).

The Working Party members were involved in collaborative work for calibration of the 8th, 9th, 10th and 11th British Standard Plasma Standards and also in calibration of the International Reference Preparation for factor VIII-related activities in plasma.

In collaboration with the I.C.T.H. Subcommittee on factor VIII the Working Party members carried out a survey in the U.S.A. and Europe of the labelled potency of factor VIII concentrates compared with potency found by the user. The results of the survey were published in Thrombosis and Haemostasis as an I.C.T.H. Report (Thrombosis and Haemostasis 1983, 50, 753-754).

Plans to carry out a comparative study of aluminium hydroxide adsorption versus barium citrate adsorption in the 2-stage assay of factor VIII were abandoned when it became apparent that barium citrate was not a convenient alternative to $Al(OH)_3$ and had problems of its own.

Much has been learned from the collaborative calibration studies about the effects of $Al(OH)_3$ adsorption on the 2-stage assay of factor VIII and it is now generally agreed that probably 10% of the discrepancies seen between 1-stage and 2-stage assays of concentrate is caused by the adsorption step. The remaining discrepancy of approximately 10% is still unaccounted for but probably has several components, including difference in reagents used as well as the unitage placed on the local plasma standard used.

With the improvement in the standards for factor VIII assay and better understanding of the discrepancy between 1-stage and 2-stage assays, the Working Party has to a large extent achieved

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The objectives laid down at its first meeting. Accordingly it has been agreed that the Working Party should be disbanded but should be reformed should any particular problem relating to the assay of factor VIII:C emerge.

As a final project the Working Party has repeated the survey carried out in 1978 to find out what changes have taken place at Haemophilia Centres, Blood Transfusion Centres and Fractionation Laboratories with regard to factor VIII assay in the past 5 years.

The results of this survey have not yet been completely analysed but a brief outline of the significant difference between the present survey and the previous one is given here.

Of the 138 questionnaires sent out 110 (80%) were returned giving a response rate almost identical to that of the previous survey. Eighty eight of the responders were Haemophilia Centres, 18 were Blood Transfusion Centres, 3 were Fractionation Centres and 1 was NIBSC.

Ninety eight of the responders said that they performed factor VIII:C assays. Of the 12 which did not (8 BTS, 4 HC), only 3 replied that they were deterred by lack of reagents. Compared with the previous survey, a large proportion of haemophilia centres are using both one and two-stage assays and fewer are using two-stage alone; proportion of laboratories using locally prepared substrate plasma or Dade substrate is less than previously and the proportion using Immuno substrate has doubled; a greater proportion are using kits for assay; a slightly higher proportion are using NIBSC standards either as working standard or to calibrate local standard; a much higher proportion stated they had no quality control problem; majority calculate results graphically though compared with previously more (23% v 8%) are using programmed calculation.

C.R. Rizza
Oxford Haemophilia Centre

13th September, 1984.

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