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Report on the Second Session of the Subcommittee on Serology and Laboratory Aspects

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EXPERT COMMITTEE ON VENEREAL INFECTIONS AND TREPONEMATOSES

Second Session of the Subcommittee on Serology and Laboratory Aspects

Members :

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Dr. I. N. Orpwood Price, Director, Venereal Diseases Reference Laboratory (Public Health Laboratory Service), St. Peter's Hospital, London, United Kingdom (*Vice-Chairman*)

Dr. F. Rappaport, Chief of Laboratories, Municipal and Beilinson Hospitals, Tel Aviv, Israel

Dr. K. V. Venkatraman, Serologist to the Government of India, School of Tropical Medicine, Calcutta, India (*Rapporteur*)

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Dr. T. Guthe, Chief, Venereal-disease Section, WHO

Dr. P. Krag, Venereal-disease Section, Laboratory and Serology Aspects, WHO (*Secretary*)

The report on the second session of this subcommittee was originally issued in mimeographed form as document WHO/VD/73, 28 November 1950.

EXPERT COMMITTEE ON VENEREAL INFECTIONS AND TREPONEMATOSES

Report on the Second Session of the Subcommittee on Serology and Laboratory Aspects [1] [2]

1. Introduction

By invitation of the Chairman, Dr. Mary Pangborn, Division of Laboratories and Research, New York State Department of Health, Albany, N.Y., USA, and Dr. C. Rein, Associate Clinical Professor of Dermatology and Syphilology, New York University Bellevue Medical Center, N.Y., USA, attended several meetings. These consultants were participating in the WHO Syphilis Seminar held concurrently in Paris.

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[1] The Executive Board, at its seventh session, adopted the following resolution:

The Executive Board,

Having considered the report of the Subcommittee on Serology and Laboratory Aspects of the Expert Committee on Venereal Infections and Treponematoses on its second session and the recommendations presented by the expert committee itself,

1. THANKS the members of the committee for their work;
2. AUTHORIZES the publication of the report;
3. ENDORSES the recommendations that descriptions of cardiolipin and lecithin be included in the *Pharmacopoea Internationalis* and that preliminary standards for cardiolipin and lecithin be established;
4. WELCOMES the appropriate steps taken by the Expert Committees on the Unification of Pharmacopoeias and on Biological Standardization in this respect;
5. ACCEPTS postponement of the International Serodiagnostic Laboratory Conference until pilot experiments on the usefulness of freeze-dried sera for evaluation of serological tests have been studied, realizing that the plans for the conference might be changed if dried reference sera of various levels of sensitivity from syphilitics and non-syphilitics are proved to be valuable for an estimate of the merit of serological tests;
6. NOTES that the pilot study is under way;
7. DRAWS ATTENTION to the progress of the inter-laboratory work on exchange of samples, and
8. ENDORSES the convening of the Subcommittee on Serology and Laboratory Aspects in 1952.

(Resolution EB7.R66, *Off. Rec. World Hlth Org.* 32)

[2] In order to avoid delays in the consideration of the report, the members of the Expert Committee on Venereal Infections and Treponematoses were consulted by mail, and unanimously agreed upon the resolutions contained in Annex 2, page 27.

Dr. E. H. Hermans, Medical Director, Anti-Venereal-Disease Association, Rotterdam, Netherlands, attended one meeting as an observer from the Expert Committee on Venereal Infections and Treponematoses.

Dr. A. A. Miles, Director, Department of Biological Standards, National Institute for Medical Research (Medical Research Council), London, United Kingdom, attended several meetings as representative of the Expert Committee on Biological Standardization.

Dr. J. A. Lorenzo, Director, Central Laboratory of Serology, Ministry of Public Health, Montevideo, Uruguay, appointed by the Uruguayan Ministry of Public Health as its observer, attended several meetings.

The subcommittee unanimously elected Mr. A. Harris as Chairman, Dr. I. N. Orpwood Price as Vice-Chairman, and Dr. K. V. Venkatraman as Rapporteur. The proposed agenda was adopted at the opening meeting. Fifteen meetings were held and the report was approved by all members.

2. Developments and Perspectives

The Expert Committee on Venereal Infections reiterated in 1949 [3] its previous opinion that any sound venereal-disease-control programme is dependent to a major degree on the efficient conduct of serological tests for syphilis, and pointed out the great lack of uniformity of procedure, technique, and the manner of reporting results in serological studies. The Subcommittee on Serology and Laboratory Aspects of the above committee endorsed this view at its first session.[4] After having re-examined the situation, the subcommittee agreed that its work should proceed on the basis of this declaration and that the chief work in the coming year should be to advise WHO on such further activities as could contribute to more efficient and uniform performance of serology in syphilis, nationally, as well as internationally.

The preparatory work for the holding of the International Serodiagnostic Laboratory Conference in 1951 had proceeded in 1949 and 1950 along the lines originally drawn up by the main committee [5] and developed in further detail by the subcommittee at its first session,[6] as approved by the fifth session of the Executive Board [7] and the Third World Health Assembly.[8]

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[3] *World Hlth Org. techn. Rep. Ser.* 1950, **13**, 23
[4] *World Hlth Org. techn. Rep. Ser.* 1950, **14**, 6
[5] *Off. Rec. World Hlth Org.* **8**, 63; **15**, 24
[6] *World Hlth Org. techn. Rep. Ser.* 1950, **14**, 6
[7] *Off. Rec. World Hlth Org.* **25**, 12
[8] Resolution WHA3.37, *Off. Rec. World Hlth Org.* **28**, 28

Certain developments have, however, taken place, and freeze-drying techniques are currently being used in the preparation of standard sera used in the international standardization of various methods and products. These refined techniques have not, as yet, been applied in an effort to establish a collection of syphilitic sera at various levels of reactivity from different stages of syphilis, or from different types of false-positive reactors. Should it be possible to use such sera as preliminary standards, this might alter several important problems connected with the planning of the International Serodiagnostic Laboratory Conference. Until preliminary studies on the possibility of establishing such a collection of dried sera have been carried out, the further detailed planning and organizational work for the conference might therefore be postponed.

The subcommittee also reviewed briefly the technical advances relating to treponematoses other than syphilis, as well as those pertaining to gonorrhoea and the minor venereal infections, which have taken place since the first session of the subcommittee. It was observed that several developments might merit consideration by the subcommittee at a later stage :

(1) the laboratory aspects of lymphogranuloma venereum ;

(2) the maintenance of live *Treponema pallidum* outside of human or animal hosts : recent claims for successful cultivation of treponema on artificial media ; studies of the life-cycle of *T. pallidum* ; and the results obtained in the differentiation studies carried out by means of the electron microscope technique ;

(3) further results available on immunological relationship between the treponemes of syphilis, yaws, bejel, and pinta, and between strains of *T. pallidum* itself ;

(4) the applicability of the Nelson test to studies on immunological changes in man and animal in relation to treatment ;

(5) the discovery of phosphatidic acid antigens other than cardiolipin.

The subcommittee reviewed further the serology and laboratory aspects of venereal diseases and treponematoses as applied to the WHO programme and activities in 1949 and 1950, and considered carefully the documentation made available to the members before and during the second session. Much of this information had been requested by the subcommittee at its first session as supporting documentation to the agenda of the second session.

This documentation included data on the inter-laboratory test evaluation being carried out between the Statens Seruminstitut, Copenhagen, Denmark, the Institut Pasteur, Paris, France, the Venereal Diseases

Reference Laboratory (Public Health Laboratory Service), St. Peter's Hospital, London, United Kingdom, and the Venereal Disease Research Laboratory (US Public Health Service), Communicable Diseases Center, Chamblee, Ga., USA (formerly Staten Island, N.Y.); the serological work of the WHO-supported venereal disease demonstration team in Simla, India; the deteriorating effect of transportation on samples; laboratory errors; as well as the plans for the studies of the investigative International Treponematosis Laboratory Centre, Johns Hopkins University, Baltimore, Md., USA.

Several WHO teams have started their activities during the last few months or preliminary surveys have been undertaken for the establishment of team centres. During the next few years, as techniques are adapted to tropical conditions and environments, serological methods will be used under difficult conditions which have not as yet been completely explored; factors giving rise to false-positive reactions will be further studied. These teams will make available technical data not only on the serological aspects of syphilis under varied and varying conditions, but will also provide WHO with information on yaws and bejel, furnishing—at little extra cost—valuable basic material for the comparative study of the biological and immunological characteristics and relationship of the treponemal diseases and their causative agents. Initial experience has shown that laboratory specimens and animals can now be sent from teams in different regions to the International Treponematosis Laboratory Centre in Baltimore for treponema immobilizing antibody tests, thus enabling the international treponematoses study to proceed along the lines recommended during the first session of the subcommittee,[9] and approved by the Expert Committee on Venereal Infections during its third session in 1949.[10]

3. International Serodiagnostic Laboratory Conference

The subcommittee discussed in detail the report on its first session [11] and the comments of the Expert Committee on Venereal Infections on this report.[12] Since the first session of the subcommittee, WHO had collected extensive information on the possible accommodation for the International Serodiagnostic Laboratory Conference. WHO had also notified Member States of the holding of the conference in 1951 in accordance with the resolution adopted by the Executive Board at its fifth session,[13] and on

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[9] *World Hlth Org. techn. Rep. Ser.* 1950, **14**, 17
[10] *World Hlth Org. techn. Rep. Ser.* 1950, **13**, 16
[11] *World Hlth Org. techn. Rep. Ser.* 1950, **14**
[12] *World Hlth Org. techn. Rep. Ser.* 1950, **13**, 23
[13] *Off. Rec. World Hlth Org.* **25**, 12

the basis of the inclusion of this activity in the 1951 budget as approved by the Third World Health Assembly [14] and the sixth session of the Executive Board.[15] An outline of the conference had been published by the medical press and preliminary applications for participation in the conference had now been received by WHO.

It was further noted that the need for sound statistical considerations during the planning stages of the conference and in the evaluation of the results obtained had been met by the Director-General.

3.1 *Considerations*

The subcommittee wished to reiterate its previous opinion that a conference would be a valuable means of evaluating the relative efficiency of serological tests for syphilis. A conference, aiming at the international standardization of serodiagnostic laboratory procedures, would also provide an opportunity for the rapid and easy exchange of scientific information by demonstrations and discussions of the attending author serologists.

The subcommittee noted that:

(1) funds at present available would allow the participation of only 15 testing teams while approximately 27 preliminary applications, representing 40 different methods, had been received from test authors;

(2) it would be difficult to evolve an acceptable scientific basis for limiting the number of participants and selecting the most desirable tests for the conference;

(3) although the use of cardiolipin antigens had increased during the past year, many laboratories had not as yet acquired experience in their use, and several new tests, or modifications of old tests, could be expected to be published during the year, which indicated that the difficulties in selecting tests for the conference would be greater than foreseen a year ago;

(4) freeze-dried serum samples might serve as suitable controls or substitutes for whole blood in evaluating relative test efficiencies; the capacity of these preparations to serve in this way could be ascertained with little expense within six months by preliminary investigations.

The subcommittee considered point (4) in detail and discussed the possible usefulness of establishing a collection of freeze-dried sera at various levels of reactivity from various stages of syphilis and from different

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[14] Resolution WHA3.64, *Off. Rec. World Hlth Org.* **28**, 39

[15] Resolution EB6.R22, *Off. Rec. World Hlth Org.* **29**, 10

types of false-positive reactors. The use of samples of such sera might serve as a means for the selection of the soundest and most suitable tests for participation in the conference.

It has been difficult with previous technical procedures to maintain the stability of weakly positive sera and many types of false-positive sera in dried form. The representative of the Expert Committee on Biological Standardization advised that methods for freeze-drying of sera were now available which had not so far been applied to syphilitic sera. The sub-committee welcomed the suggestion that a pilot study be established to determine whether serum samples, dehydrated according to such methods, will meet the primary requirements of complement-fixation and flocculation tests for syphilis. An outline for the conduct of such a pilot study is attached to this report.[16] This outline was prepared and recommended by the representative of the Expert Committee on Biological Standardization on the understanding that it be carried out in co-operation with the Statens Seruminstitut, Copenhagen, and the following six laboratories:

Institut Pasteur, Paris, France

School of Tropical Medicine, Calcutta, India

Municipal and Beilinson Hospitals, Tel Aviv, Israel

Gade's Institute, University of Bergen, Norway

Venereal Diseases Reference Laboratory, St. Peter's Hospital, London, United Kingdom

Venereal Disease Research Laboratory, Communicable Diseases Center, Chamblee, Ga., USA.

The pilot study should be restricted to 12 donor sera and the findings and reports on the project made available within the next six months. The pertinent observations are to be returned to the Secretary of the sub-committee for analysis and for distribution to the members of the sub-committee and participating laboratories, to the members of the Expert Committee on Venereal Infections and Treponematoses, and to the members of the Expert Committee on Biological Standardization, for further consideration.

Should this pilot study yield *encouraging*, but not entirely *satisfactory*, results, a further study should be undertaken to investigate the factors adversely affecting the study and the possible improvements in technique which could be made to establish stable dried syphilitic sera of various reactivity levels.

Should the results obtained be *satisfactory*, they would justify a large-scale collection of freeze-dried sera from different stages of treated and

[16] Annex 1, page 23