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EXPERT COMMITTEE
ON VENEREAL INFECTIONS

Report on the Third Session

Washington, D.C., 10-20 October 1949

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EXPERT COMMITTEE ON VENEREAL INFECTIONS

Third Session

Members :

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- Dr R. Degos, Professeur agrégé à la Faculté de Médecine de l'Université de Paris, France
- *Dr M. Grzybowski, Professor of Dermatology, Director, Clinic of Dermatology and Syphilology, University of Warsaw, Poland
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- Dr E. H. Hermans, Medical Director, Anti-Venereal-Disease Association, Rotterdam, Netherlands
- Dr G. L. M. McElligott, Director, Venereal Disease Department, St. Mary's Hospital ; Adviser in Venereal Diseases, Ministry of Health, London, United Kingdom (*Rapporteur*)
- Dr J. F. Mahoney, Chief, Laboratory of Antibiotic Research and Development, Section of Laboratory of Infectious Disease, Microbiological Institute, National Institutes of Health (US Public Health Service), Staten Island, N.Y., USA (*Chairman*)
- Dr I. H. Nagi, Director, Venereal Diseases Section, Ministry of Public Health, Cairo, Egypt
- Dr R. V. Rajam, Professor of Venereology, Government General Hospital, Madras, India (*Vice-Chairman*)

Consultants :

- Dr N. R. Ingraham, Chief, Division of Venereal Disease Control, Department of Public Health, Philadelphia, Pa., USA
- Dr P. V. Marcussen, Physician in charge, Venereal Disease Clinic, Kommunehospitalet, Copenhagen, Denmark ; Chairman, WHO Syphilis Study Commission to the USA
- Dr E. W. Thomas, Professor of Clinical Medicine, New York University College of Medicine ; Director, Rapid Treatment Center, Bellevue Hospital, New York City, N.Y., USA

Observers :

- Dr G. E. Samame, Venereal Disease Consultant, Pan American Sanitary Bureau, Washington, D.C., USA
- Dr P. Sanchez, Chief, Venereal Disease Division, Department of Health, Caracas, Venezuela
- Dr W. F. Snow, President, International Union against Venereal Diseases, New York City, N.Y., USA
- A. Woodchek, International Labour Office, Washington, D.C., USA

Secretariat :

- Dr T. Guthe, Chief, Venereal Diseases Section, WHO (*Secretary*)
- Dr A. Spillmann, Regional Adviser on Venereal Diseases for Europe, WHO

The report on the third session of this committee was originally issued in mimeographed form as document WHO/VD/54, 10 November 1949.

* Indicates member unable to attend.

COMMENTS BY THE EXECUTIVE BOARD

The Executive Board, at its fifth session, examined the report of the Expert Committee on Venereal Infections on its third session and expressed its appreciation of the work done by the experts serving on the committee. The Board noted with approval the policy recommended by the committee of stimulation of the training of personnel for administrative, clinical, and laboratory purposes, without which an appropriate structure could not be developed, and the emphasis placed on teaching and training through support of national training institutions in regions where only limited facilities exist. The maintenance of balance between specialized programmes and an overall programme of disease prevention was endorsed. The Board agreed that stimulating governments to develop integrated health activities in such a way that programmes might continue to operate when outside assistance was withdrawn was basically sound. The importance of WHO proceeding cautiously towards the long-term objectives set forth in its programme for 1950 was emphasized. Agreement was expressed with the idea that WHO should continue to make available to health administrations venereal-disease literature, technical releases, and reference lists on clinical, epidemiological, and other aspects of venereal-disease control.

The Board emphasized the importance of the committee's recommendation on the epidemiological aspects of venereal-disease control, particularly as related to maritime aspects and port and river projects, and of the exchange of epidemiological information between maritime countries and major ports.

The Board noted the demonstrated uniform response of the various treponematoses of syphilis, yaws, pinta, and bejel to penicillin, and also the development of new techniques permitting study of the biological and immunological relationship between the causative agents of the different treponematoses. Various limited projects had been carried out in different parts of the world using a mass approach based on penicillin, and the time appeared to have come for a larger project in a geographically delimited area with a high prevalence of disease. The opinion of the experts that Haiti was a suitable island for such an activity was endorsed. The Board further noted that the proposed project had the full support of the Haitian Government, the United Nations Children's Emergency Fund (UNICEF), and WHO.

The Board was of the opinion that an expert committee on treponematoses and venereal infections should be formed, merging the existing Expert Committee on Venereal Infections with the Expert Committee on Treponematoses proposed under the Technical Assistance Programme for 1950, with appropriate study-groups or subcommittees as required for specific sectors.

EXPERT COMMITTEE ON VENEREAL INFECTIONS

Report on the Third Session¹

1. INTRODUCTION

The third session of the Expert Committee on Venereal Infections was held in Washington, D.C., USA, from 10 to 20 October 1949. By invitation of the Chairman, members of the Subcommittee on Serology and Laboratory Aspects² and of the WHO Syphilis Study Commission to the USA³ attended several meetings. Dr T. J. Bauer, Medical Director, Chief, Division of Venereal Disease, US Public Health Service, Washington, D.C., USA, Dr E. G. Clark, President, Executive Committee, American Venereal Disease Association, and Dr J. E. Moore, Chairman, Subcommittee on Venereal Diseases, National Research Council, Baltimore, Md., USA, were also present.

The committee unanimously elected Dr J. F. Mahoney as Chairman, and Dr R. V. Rajam as Vice-Chairman. Dr G. L. M. McElligott was elected Rapporteur.

The provisional agenda was adopted with minor modifications. Special attention was paid to the committee's relationship with the Subcommittee, on Serology and Laboratory Aspects, which was holding its first session from 12 to 20 October 1949. In approving the agenda of the subcommittee, it was decided that Dr P. V. Marcussen, co-opted consultant of the main

¹ The Executive Board, at its fifth session, adopted the following resolution :

The Executive Board

(1) NOTES the report of the Expert Committee on Venereal Infections on its third session ; and

(2) AUTHORIZES its publication ;

Taking into account the recommendations of the expert committee in considering relevant items on its agenda,

(3) TRANSMITS the report to the Third World Health Assembly ; and

(4) POINTS OUT that recommendations of expert committees which concern WHO policy and operations remain recommendations except as they are implemented by the Executive Board or the World Health Assembly in adopting and putting into action the annual programme of WHO.

² See *World Hlth Org. techn. Rep. Ser.* 1950, 14.

³ See *World Hlth Org. techn. Rep. Ser.* 1950, 15.

committee, should act as liaison in matters of clinical syphilis in relation to serology and laboratory aspects.

The terms of reference of the subcommittee, proposed in general terms by the previous two sessions of the main committee and approved by the Executive Board and the World Health Assembly, were more specifically defined as follows :

(1) to advise on matters relating to the organization of the international serodiagnostic laboratory conference, approved by the Health Assembly, and to propose plans for this conference, including objectives, technical operation, and timing ; and further

(2) to advise on other matters on the agenda, particularly the comparative treponematoses study proposed in the WHO bejel project.

The committee considered its relationship with the WHO Syphilis Study Commission to the USA, and noted the terms of reference of this commission. It was agreed that the statement of the commission to the Expert Committee on Venereal Infections be presented to the fifth session of the WHO Executive Board, to be held in January 1950, together with the report of the committee.

The committee noted the approval by the Executive Board of the report on the second session of the ad hoc Expert Committee on Venereal Diseases,⁴ and the observations made by the Board.⁵ The committee noted further the resolution of the Executive Board at its fourth session on local application of the Brussels Agreement in the Rhine River Area.⁶

The committee established a working party, consisting of Dr W. E. Coutts, Dr E. H. Hermans, and Dr G. L. M. McElligott as members, and Dr N. Jungalwalla and Dr T. Putkonen as consultants, to consider the maritime aspects of venereal-disease control in general, and the projected revision of the Brussels Agreement as part of future international health regulations for venereal-disease control in particular, to study agenda items relating to these subjects, and to report and make recommendations to the main committee.

The committee considered carefully extensive documentation, made available before and during the session, relating to the development of the WHO venereal-disease programme, the present and the projected scope of the work, as well as other supporting documentation. In discussion, major emphasis was placed on technical orientation, the programme elements and general outlook of WHO in venereal-disease control

⁴ *Off. Rec. World Hlth Org.* 15, 18

⁵ *Off. Rec. World Hlth Org.* 14, 19

⁶ *Off. Rec. World Hlth Org.* 22, 2, 16

having already been considered at the first and second sessions of the committee. Control techniques, the statement of the WHO Syphilis Study Commission to the USA,⁷ antibiotic therapy in syphilis and related diseases, and serology and laboratory aspects including the report of the Subcommittee on Serology and Laboratory Aspects,⁸ were considered at length by the committee.

An effort has been made to avoid as far as possible reiteration of still valid considerations set forth in the previous reports of the committee.⁹

2. DEVELOPMENTS AND PERSPECTIVES

2.1 WHO Venereal-Disease Activities¹⁰

The development in each individual country, within the framework of the health administration, of a venereal-disease control structure permitting a maximum degree of control should remain one of the aims of WHO. The larger reservoirs of syphilis and other venereal diseases are found in less-developed areas where venereal-disease activities have been organized only to a limited extent. A high priority should be given by WHO to assistance to countries in such areas, and emphasis should continue to be placed in the WHO venereal-disease programme in 1950 and 1951 on early syphilis of the sporadic or endemic type.

At the request of health administrations, WHO should continue to assist countries with advisory and demonstration services, and to stimulate the training of personnel for administrative, clinical, and laboratory purposes, without which a permanent control structure cannot be developed. In its assistance programme, emphasis should be placed on teaching and training through support of national training institutions in regions where only limited facilities exist. Although requirements vary, support of national training institutions by WHO in the form of teaching equipment, supplies, and literature, as well as by provision of temporary consultants,

⁷ *World Hlth Org. techn. Rep. Ser.* 1950, 15

⁸ *World Hlth Org. techn. Rep. Ser.* 1950, 14

⁹ *Off. Rec. World Hlth Org.* 8, 60; 15, 18

¹⁰ The Executive Board, at its fifth session, adopted the following resolution:

The Executive Board

(1) APPROVES the recommendation of the expert committee on venereal-disease activities, developments and perspectives of WHO (subsection 2.1 of the report); and

(2) EMPHASIZES the importance of priority being given to economically under-developed areas with a high prevalence of venereal disease (and/or other treponematoses).

teaching staffs, and travelling seminars composed of highly specialized experts, would accelerate the establishment of this programme, particularly when co-ordinated with venereal-disease-control training courses under the WHO fellowship programme. Wherever possible, such training activities should be developed into broader programmes for postgraduate work in public health.

Any group of public-health workers who attain a high degree of specialization may tend to overlook the fact that in the final analysis their work will prove productive only if supported by a general programme of disease prevention. Isolated efforts directed towards specific problems as a rule will have difficulty in surviving unless integrated in an overall programme. At present WHO teams devoted to venereal-disease control are in a position to enter the field with a minimum of preparation and to assist in the organization of control measures with a minimum of delay, financial outlay, and scientific personnel. The start made by venereal-disease workers should be followed as soon as possible by other equally important, but sometimes less flexible, public-health and sanitation activities. The committee is fully aware of the similar functions to be ascribed to spearheads, represented by malaria, tuberculosis, and other specialized programmes; similar extensions into broader public-health programmes can equally well take place where these diseases are prevalent. There is no doubt, however, of the appeal of syphilis in pregnancy and congenital syphilis in all venereal-disease programmes. In conjunction with activities devoted to the furthering of maternal and child health, measures to be taken should be aimed at the identification of the disease in women, and the provision of adequate therapy and postpartum observation of mother and child. In addition, visits to the family by the physician, nurse, health educator, or social worker permit scrutiny of the syphilitic status of the other family members and the taking of necessary steps to prevent reinfection. This approach may in some areas represent a basis for a wider understanding of the general epidemiological principles of case-finding and contact investigation in venereal-disease control. Wherever venereal-disease teams are assigned to work with health administrations in the field, paediatric personnel, health educators, etc., should be introduced as soon as possible after the initiation of anti-venereal-disease activities.

Another natural development would be the combination of antisyphilis programmes with measures against other treponematoses, where these are prevalent. The general vulnerability of the causative agents of yaws, bejel, and pinta to penicillin attack has been discussed elsewhere. Joint projects with tuberculosis, malaria, and other field units should be undertaken, wherever possible, when initial mass examinations offer administrative as well as public-health advantages.

In areas where WHO field teams are working with health administrations in demonstration areas, operational centres and laboratory facilities should be utilized as provisional training centres, under a plan developed by the health administration and WHO, for the instruction of national trainees as well as of personnel from other countries in the region.

Ultimately, the development in demonstration areas of the full complement of public-health services would be a desideratum, a major effort being made to expand in such spearhead areas as have proved successful, and to maintain the broad gains obtained through the initiation of the activity under the leadership of the local or national health-administration.

Active case-finding aiming at the identification and prevention of syphilis in pregnant women and infants represents an important stimulating element in organized large-scale, nationwide venereal-disease-control programmes, or in maternal and child health activities on a broad scale. The committee observed with satisfaction that this outlook, as originally recommended by the committee at its second session,¹¹ has been the basis for UNICEF/WHO participation in, and encouragement of, the anti-syphilis campaigns of the national health-administrations in Bulgaria, Czechoslovakia, Finland, Hungary, Italy, Poland, and Yugoslavia. The development of these campaigns, the active part taken by WHO technical consultants in the discussion, inception and follow-up of programmes, the amount of medical literature and the number of fellowships provided by WHO, as well as the significant penicillin supplies and laboratory equipment furnished by UNICEF, were noted by the committee.

The committee agreed that stimulating governments to develop integrated health activities in such a way that programmes may continue to operate when outside assistance is withdrawn, is basically sound, and that programmes of this kind should go forward in countries where surveys have been, or are being, carried out in South-East Asia, the Middle East, and the Americas.

In many countries health administrations and national institutions have limited access to venereal-disease literature. Experience has shown that the time required for important contributions to appear in print and be distributed often represents an important delay in the acquirement of information on recent technical developments. With the very rapid technical development in the therapeutic and laboratory aspects of venereal-disease control, such as penicillin in syphilis and cardioliipin-lecithin

¹¹ *Off. Rec. World Hlth Org.* 15, 25

antigens in serodiagnosis, this situation is considered to be of some significance. WHO should, therefore, continue to be of assistance to health administrations and national institutions in this question. Corresponding members of the committee could assist in bringing major developments in individual countries to the attention of WHO.

The committee adopted the following resolution :

The Expert Committee on Venereal Infections

Considering the long- and short-term objectives of WHO in venereal diseases, as set out in the 1950 programme,¹²

RECOMMENDS

- (1) that WHO proceed cautiously towards the long-term objectives, and that priority be given to economically underdeveloped areas with a high prevalence of syphilis and/or other treponematoses ;
- (2) that the 1950 programme form the basis for activities in 1951 and 1952, so as to enable consolidation of the gains obtained ; development of polyvalent services in nationwide programmes and in demonstration areas following initial venereal-disease operational activities is desirable ; with particular emphasis on maternal and child health, and health education ;
- (3) that emphasis be placed on assisting countries to establish in their health administrations at least a basic venereal-disease control structure headed by a health officer specializing in venereal-disease control ;
- (4) that WHO support selected venereal-disease training activities in regions where limited facilities are available, and the setting-up of regular training courses in training institutions under an organized fellowship programme, preferably where such a programme can become part of an overall public-health educational system ;
- (5) that WHO encourage the establishment of venereal-disease literature units in health administrations and other suitable institutions ; and continue to prepare and distribute to such units, under the WHO literature programme, venereal-disease literature, technical releases, and reference lists on clinical, epidemiological and other aspects of venereal-disease control ;
and
- (6) that the Director-General appoint further corresponding members in different countries, and that these members make available to WHO and committee members information on major technical developments in their respective countries.

¹² *Off. Rec. World Hlth Org.* 18, 86

2.2 International Health Regulations and Maritime Aspects of Venereal-Disease Control¹³

Following the postwar peak in 1946/47, the incidence of venereal disease, particularly early syphilis, declined significantly in some areas of the world, notably Australia, Europe and North America. The extent of this fall has been less marked in seaports than in inland areas. An entirely different situation exists in other regions of the world, and important foci of syphilis and gonorrhoea remain in many less-developed areas, possibly on a larger scale than before. With industrial development envisaged in these areas and a further increase in maritime communications, the chances of introducing venereal infections from areas of high to areas of lower prevalence are increased. In noting the unavoidable delays in the development of international health regulations for venereal-disease control, the principles of which have been approved by the Health Assembly, the necessity is emphasized for interim measures in relation to the Brussels Agreement of 1924 relating to treatment facilities for seafarers. This agreement remains the sole practical instrument for venereal-disease control between countries. Of the present 56 signatories to the agreement there are only 21 States, 20 of which are Members of WHO, the remainder of the signatories being individual island groups, dependencies, or special ports.

The committee wished to reiterate its previous statement concerning the importance of collection of basic data on venereal-disease morbidity. Notification by physicians as well as medical institutions to the health administration for statistical purposes should be adopted by countries as a routine procedure, at least as far as primary and secondary syphilis and infantile congenital syphilis are concerned. Such data should be available also in regard to nationality of cases thus recorded, so that health administrations can obtain information on the possible reservoir of infection among nationals outside the country, in the case of maritime countries forming part of their maritime population.

Recognizing the interference of venereal diseases in the working capacity of maritime and industrial populations, the committee noted the special

¹³ The Executive Board, at its fifth session, adopted the following resolution :

The Executive Board

(1) APPROVES the recommendation of the expert committee regarding international health regulations and maritime aspects of venereal-disease control (subsection 2.2 of the report) ;

(2) CALLS the attention of Member Governments to the importance of more countries adhering to the International Agreement of Brussels and to the establishment of venereal-disease programmes in major ports ; and

(3) REQUESTS the Director-General to take the necessary steps for the early publication and distribution of the revised edition of the individual treatment booklet and the WHO international venereal-disease treatment centre list.

interest shown by the International Labour Organization (ILO) and the International Union against Venereal Diseases, and their co-operation with WHO, particularly in regard to the Rhine River project, which emphasizes further the need for international co-operative undertakings in this field.

While the introduction of almost immediate sterilizing therapy for gonorrhoea and syphilis, and the increasing application of ambulatory treatment based on repository penicillin preparations, may make it possible, depending upon the nature of each individual case, to retain seafarers and watermen aboard ship after initial treatment by a physician, there has on the other hand been an increasing tendency for treatment to be undertaken aboard ship by untrained personnel, without diagnosis. This practice is being encouraged by the carrying of authorized or non-authorized penicillin supplies for emergency or other purposes. This procedure is responsible for the loss of valuable epidemiological information and poor follow-up of the patient.

The committee adopted the following resolution :

The Expert Committee on Venereal Infections

Having studied the report of the working party set up to consider the question of international health regulations and maritime aspects of venereal-disease control,¹⁴

RECOMMENDS

(1) that WHO draw the attention of governments to the desirability of more countries adhering to the Brussels Agreement, whilst awaiting the establishment of wider international regulations for venereal-disease control, and that :

(a) steps be taken for the publication and distribution by WHO early in 1950 of the revised edition of the individual treatment booklet ;

(b) a revised edition of the list of international treatment centres for venereal diseases be made available as widely as possible and distributed in printed form early in 1950 to health administrations, port authorities, and other interested parties ;

(2) that the draft text of the international health regulations for venereal-disease control be established as soon as possible for circulation to governments, with emphasis on the following principles :

(a) free therapy for venereal diseases to be available at the treatment centres of all Member States of WHO, regardless of nationality of the patient ;

¹⁴ Unpublished working document WHO/VD/53

- (b) infectious syphilis to be included among the diseases notifiable for statistical purposes to national health-administrations by physicians as well as medical institutions ;
- (3) that consideration be given to the establishment of a subcommittee consisting of four members to act as a technical consultative body for the application of the projected international health regulations for venereal-disease control when these come into force in 1951 or 1952 ;
- (4) that venereal-disease-control demonstration projects be established in major ports, especially in underdeveloped areas, and that such activities be given a high priority in the WHO venereal-disease programme, should funds from the Technical Assistance Programme of the United Nations be available in 1950 and 1951 ; and
- (5) that liaison be maintained between the Expert Committee on Venereal Infections and the Joint ILO/WHO Committee on the Hygiene of Seafarers.

2.3 Treponematoses¹⁵

At the previous two sessions of the committee it was agreed that major attention should be concentrated in the WHO venereal-disease programme on early infectious syphilis and prenatal and infantile syphilis, using modern public-health methods, and that work directed against other venereal infections should be considered when they constitute a special public-health problem in a geographical area, or where spread of disease from country to country is involved. It may appear desirable to give more detailed attention to the prevention of the late manifestations of syphilis. While the reduction of the damaging effects of late disease upon the central nervous system and the vascular system constitutes an ultimate public-health objective, it may best be attained through an attack upon early infections. The relative infrequency with which these complications are observed would appear to make it inadvisable at this time to divert available

¹⁵ The Executive Board, at its fifth session, adopted the following resolution :

The Executive Board

- (1) APPROVES the recommendations of the expert committee regarding treponematoses (subsection 2.3 of the report) ;
- (2) REQUESTS the Director-General to give full support to the syphilis-yaws project in the island of Haiti and the Dominican Republic and the WHO bejel project in the Eastern Mediterranean area ; and
- (3) RECOMMENDS that an Expert Committee on Treponematoses and Venereal Infections should be formed, merging the existing Expert Committee on Venereal Infections with the Expert Committee on Treponematoses proposed under the technical assistance programme for 1950, with appropriate study-groups or sub-committees as required in the specific-sectors.

resources to a special consideration of the prevention and medical care of the effects of late syphilis. The original concept, therefore, remains sound, but several developments have occurred justifying a broader consideration of the entire group of treponematoses, not only of syphilis. These include :

(1) Technical considerations :

(a) The demonstrated uniform response of various treponematoses, such as syphilis, yaws, pinta, and bejel, to penicillin ;

(b) the development of treponemal antibody techniques of Turner and Nelson, permitting study of the biological and immunological relationship between the causative agent of the various treponematoses in man and animals ;

(c) the recent support given to the identification of bejel as an endemic syphilitic disease.

(2) Administrative considerations :

(a) the referring of treponematoses other than syphilis, notably bejel and yaws, by the Executive Board and the Health Assembly, to the Expert Committee on Venereal Infections for consideration ;¹⁶

(b) the decision of the Second Health Assembly to establish in 1950, under the expanded technical assistance programme of WHO, an expert group on treponematoses composed of 9 members including 3 syphilis experts of the present Expert Committee on Venereal Infections.¹⁷

It is recognized that treponemal diseases other than syphilis, particularly yaws, in themselves impose a serious social and economic burden upon countries where these diseases are endemic. Extensive endemic foci have been known to exist for decades in the tropical Americas, Africa, Asia, and in many islands of the Pacific. The multitude of names given to the various manifestations in these areas testify to the universality of the disease. The hypothesis of Hudson holds that the various treponematoses, syphilis included, are caused by the same organism in the various parts of the world but exhibit different clinical and epidemiological patterns as a result of different environmental factors. The varieties comprise the sporadic syphilis of the temperate zones with its sexual transmission, tending to involve mucous surfaces with periods of latency and the ability to invade the vascular system and the brain stem ; yaws, the disease of childhood in the tropics ; as well as the bejel of the desert ; the last two characterized by non-venereal transmission and surface lesions, but with little late sequelae or congenital manifestations.

¹⁶ *Off. Rec. World Hlth Org.* 17, 11; 21, 27.

¹⁷ *Off. Rec. World Hlth Org.* 21, 28

Mass application of penicillin in "eradication projects" has been carried out in limited areas in Africa (yaws) where communities enjoyed freedom from the disease over a period of months prior to re-introduction of disease; in small island groups — Pacific atolls (yaws); in a national Indian reservation in the USA (syphilis), and elsewhere. The rationale supporting the opinion that an eradication project on a larger scale be undertaken at this time is the favourable response to rapid penicillin-control techniques recently established in yaws, bejel, and pinta, which offers an opportunity to reduce significantly the toll taken by treponematoses in areas where these diseases are prevalent and active work can be undertaken by health administrations. Available techniques lend themselves to mass application, because of simplicity of method and non-toxicity of the antibiotic, and the rapid epidemiological control of the disease which follows. A large-scale project should be carried out in a geographically delimited area with a high prevalence of disease, the mass attack being based on the use of repository penicillin preparations. The envisaged project for eradication of syphilis and yaws in rural areas of the island of Haiti and of the Dominican Republic appears to fulfil these conditions, and the support of this project given by WHO, the Pan American Sanitary Bureau and UNICEF at the request of the Haitian and Dominican Republic governments is noted with satisfaction.

Like yaws, bejel is a disease predominantly affecting children but without primary manifestations, although such have been produced by the inoculation of human volunteers. Recently support has been given to the identification of bejel as an endemic syphilitic disease, non-venereally acquired. There appears to be a high prevalence of this disease in endemic areas in the Middle East, which are currently being surveyed by WHO. The social and economic burden represented by its afflicted large population groups has been pointed out by the Iraqi delegation to the first World Health Assembly, and the WHO Regional Committee for the Eastern Mediterranean recommended at its second session, held in Geneva from 12-15 October 1949, that UNICEF and WHO should support suitable programmes for combating the disease in the region, including the establishment of a demonstration area in 1950, thus meeting the request of the Government of Iraq.¹⁸

The committee considers that the bejel project for field and investigative activities proposed by the Director-General and recommended by the Regional Committee for the Eastern Mediterranean should go forward, and that the documentation in support of this project be drawn to the attention of health administrations and institutions in the region, with a

¹⁸ Unpublished working document RC2/EM/28 Rev. 1

view to further elucidation of the nature of this disease, the causative agent, *Treponema pallidum* of bejel, having so far not been isolated in the experimental animal.

Although it is recognized that syphilis, bejel, pinta, and yaws, and certain natural treponematoses of animals, are epidemiological and perhaps clinical entities, the fundamental biological relationships within the larger group is still a matter of dispute. The resolution of this question may, at first glance, seem to be of limited importance, but, considering the various syndromes from a world viewpoint, a knowledge of the basic relationship is necessary for an intelligent approach to control, for not only are there many practical ways in which such knowledge is useful, but much uncertainty and irresolution will be lifted from the minds of those who must make decisions pertaining to this large group of human disease.

WHO can make a significant contribution, at little extra cost, to the ultimate definition of the nature of treponemal diseases in man and their biological and immunological relationships by utilizing the clinical and laboratory material available from field units and by organizing participation of national laboratories in areas where treponematoses are prevalent.

Having carefully considered the relevant paragraphs of the report of the Subcommittee on Serology and Laboratory Aspects,¹⁹ and the stimulating statement of Dr T. B. Turner in this regard,²⁰ the committee is convinced that the co-operative comparative study based on the Director-General's project represents an activity worthy of WHO's attention.

The committee adopted the following resolution :

The Expert Committee on Venereal Infections

RECOMMENDS

(1) that the syphilis/yaws project in the island of Haiti and in the Dominican Republic proceed as soon as possible, and that :

(a) the technique to be used be based on procaine penicillin G in oil with 2% aluminium monostearate ;

(b) at the present stage of planning, the establishment of a sound minimum administration and other control machinery be studied, to enable health administrations, with the necessary outside assistance, to consolidate the public-health gains obtained by the initial mass approach ; considerations should include the study of measures for the prevention of reinfection ;

¹⁹ *World Hlth Org. techn. Rep. Ser.* 1950, 14

²⁰ Unpublished working document WHO/VD/50

- (c) the results obtained be carefully studied in view of the importance of the application of such public-health techniques to other areas where yaws and treponematoses are endemic ;
- (2) that the bejel project in the Eastern Mediterranean area be activated early in 1950, and that :
- (a) a preliminary field study be undertaken at that time ;
 - (b) the pilot area be established in Iraq as soon as the hot season is over ;
 - (c) the co-operative international treponematoses study go forward, and that a central guiding scientific institution be selected to initiate this study ; and
- (3) that the terms of reference of the Expert Committee on Treponematoses projected for 1950 be clarified, so as to avoid duplication of effort, or that WHO give consideration to the merging in 1951 of the existing Expert Committee on Venereal Infections with that on treponematoses, and that :
- (a) appropriate study-groups or subcommittees be constituted as required ; and that
 - (b) this question be considered further at the next meeting of the committee.

3. ANTIVENEREAL DRUGS AND THERAPY

3.1 Availability of Penicillin

The progress made and the co-operation achieved by WHO with the Economic Commissions of the United Nations in regard to the stimulation of penicillin production is noted by the committee. A study of the interim report on penicillin requirements and availability, based on the inquiry carried out by WHO at the suggestion of the original venereal-disease committee, leads the committee to agree that this study²¹ is incomplete and does not cover those areas where presumably the needs are greatest and where only limited data may be available for estimating the factual requirements. The committee considers that the study should be continued so that worldwide requirements of the drug can be further evaluated.

Activities in regard to the rehabilitation of the UNRRA penicillin plants and the recommendation for the establishment by WHO of an

²¹ Unpublished working document WHO/VD/41

expert committee on antibiotics were noted. The committee wished to reiterate its view that the limited availability of penicillin is a major restricting factor in the control of syphilis and related diseases in the world.

The work undertaken by WHO for the establishment of an international pharmacopoeia was welcomed, and it was agreed that the inclusion of basic anti-venereal-disease drugs in the *Pharmacopoea Internationalis* would be of primary importance to health workers in many lands. It was suggested that the attention of the Expert Committee on the Unification of Pharmacopoeias be drawn to the desirability of including, if possible, characteristics also of vehicles and water-repellant substances used in identifying penicillin preparations, such as procaine penicillin G in oil with 2% aluminium monostearate (PAM). Only equal characteristics of all elements in repository preparations will enable truly comparative investigations to go forward. An indication of particle size and stability is particularly desirable. The committee was aware that this suggestion introduced an extension in principle of the work now being done by the Expert Committee on the Unification of Pharmacopoeias, but believed the matter sufficiently important to bring forward this suggestion.

The committee considered that the following antivenereal drugs should be included in the *Pharmacopoea Internationalis* :

| | |
|-----------------------|-----------------|
| Arsenoxides | Streptomycin |
| Aureomycin | Sulfadiazinum |
| Neoarsphenamine | Sulfaguanidinum |
| Sodium penicillin G | Sulfathiazolum |
| Procaine penicillin G | |

3.2 Antibiotic Treatment of Syphilis and Related Diseases

The situation outlined in previous reports of the committee in relation to therapy of gonorrhoea and minor venereal diseases remains essentially the same, except in the case of lymphogranuloma venereum where initial experience indicates the beneficiary therapeutic value of aureomycin. Attention was also paid to the newer antibiotics introduced experimentally, namely, aureomycin and chloromycetin, which have been shown to possess treponemicidal activity. Knowledge at present accumulated does not indicate that they will play an immediate role in the control programme. The committee will scrutinize carefully the future development of these and similar substances with a view to their possible public-health value. An effective antibiotic orally administered might represent a development which would force alignment of the control mechanism in some geographical areas.

The committee has reviewed in considerable detail the present status of antibiotic therapy, especially the use of penicillin alone in early syphilis and prenatal and infantile syphilis, and the important development represented by the introduction of reliable absorption-delaying preparations and the results obtained with procaine penicillin G in oil with 2% aluminium monostearate. The use of penicillin in neurosyphilis and late manifestations was not considered at the present session. Participation in the discussions of the WHO Syphilis Study Commission to the USA, the terms of reference of which included the study of venereal-disease-control methods "with particular reference to penicillin treatment in syphilis",²² was highly stimulating and permitted a wide international exchange of views and experience, which emphasized the current orientation on penicillin therapy in syphilis. Data on the results obtained with procaine penicillin G with 2% aluminium monostearate in syphilis are only slowly accumulating outside the USA, and the committee welcomed particularly the contribution made by the presentation, for the first time, of case material from Europe, South America and South-East Asia.²³

True penicillin resistance has not been recorded in gonorrhoea (in vivo), syphilis or other treponematoses, which justifies the attitude that this non-toxic antibiotic should be used as widely as possible notwithstanding the recognized possibility that at some future date resistant strains of gonococci and treponemata may be observed.

The past six years' experience with penicillin therapy in syphilis has not established general agreement regarding dosage or the optimum time of treatment. Regardless of opinions on time-dose relationships, and recognizing the continued application in Europe and elsewhere of adjuvant therapy — arsenicals and/or bismuth — following initial penicillin administration, the data now available have proved beyond doubt that so far penicillin is the best single antisyphilitic agent for immediate treatment which has ever been used on a wide scale.

3.2.1 *Newer repository penicillin preparations*

3.2.1.1 *In early syphilis.* With the advent of repository penicillin preparations, further simplification of penicillin therapy has taken place. This has resulted from the ability of the newer absorption-delaying preparations of procaine penicillin G with 2% aluminium monostearate to maintain demonstrable blood-levels for prolonged periods. A single injection of 300,000 Oxford units of PAM can maintain an effective blood-level for more than 96 hours. The comparative picture of average penicillin blood-concentrations produced with single injections of six

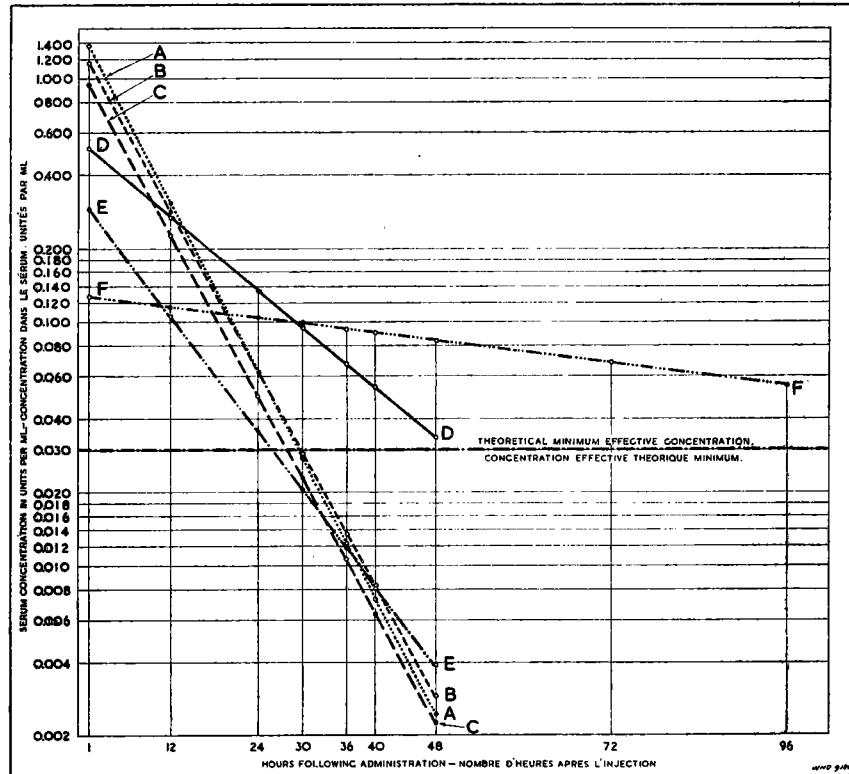
²² *World Hlth Org. techn. Rep. Ser.* 1950, 15

²³ Unpublished working documents WHO/VD/46 Rev. 1 and WHO/VD/52

previously employed repository penicillin preparations is shown in fig. 1.

There are under scrutiny by various investigators at this time several groups of patients treated for experimental purposes within one day who received either a single injection or a series of injections ranging from

FIG. 1. AVERAGE BLOOD-CONCENTRATION OF PENICILLIN



Concentrations obtained with a single injection (300,000 units) of six repository penicillin preparations, using the *Sarcina lutea* cup plate method of assay.

- A = sodium penicillin G in peanut oil with 4.8 % (w/v) white beeswax
- B = sodium penicillin G in peanut oil with 2 % (w/v) aluminium monostearate
- C = procaine penicillin G in oil
- D = procaine penicillin G (large particle size) in peanut oil with 2 % (w/v) aluminium monostearate
- E = aluminium penicillin in peanut oil with 2 % (w/v) aluminium monostearate
- F = procaine penicillin G (fine particle size) in peanut oil with 2 % (w/v) aluminium monostearate

300,000 to 600,000 Oxford units each. Treatment schemes are otherwise employed for a period of two to four weeks with injections at different time intervals for a total dosage of 1,200,000, 2,400,000 and 4,800,000 Oxford units of PAM.

The committee unanimously agreed that, in the interests of public health, prompt penicillin therapy is essential in the treatment of all cases of early infectious syphilis. Although sufficient time has not yet passed since the advent of PAM to evaluate the ultimate outcome of the disease, studies followed carefully during the last two years indicate that results to date are better than with penicillin preparations previously employed. It is remarkable that there do not appear to have occurred any completely acceptable instances of clinical central nervous system relapse in a patient receiving adequate penicillin therapy — aqueous, penicillin in oil and beeswax (POB), or PAM — in the early stages of infection. This statement is valid for a small group of patients who have been under observation for approximately seven years and for a large group of patients who have had progressively shorter post-treatment observation. In the event of this situation continuing for the coming several years, the danger of development of syphilis of the central nervous system will have largely passed. The prolonged post-treatment follow-up which is at present necessary may be curtailed and a shorter routine adopted.

The manner in which data on treatment, re-treatment, clinical and serological relapses, seroresistance, and reinfection in syphilis is recorded in penicillin case-material in relation to patient-percentage follow-up, at given intervals, over a period of time, differs from the past method of recording of such material treated with arsenicals and/or bismuth. This has made analysis of such material extremely difficult. An effort might be made to arrange and analyse material available on series of patients treated with arsenic and/or bismuth, according to the requirements now exercised in penicillin-treated material. A review of suitable material should be presented to the committee at a subsequent meeting by a corresponding study-group of three committee members, with the above points in mind.

3.2.1.2 *In prenatal and infantile syphilis.* The time to treat infantile syphilis is prenatally. Women not examined for syphilis during pregnancy should be examined at the time of delivery or at the time the infant is presented for paediatric care.

Penicillin readily permeates the placenta from the maternal bloodstream to the foetal tissues as early as the tenth week of gestation, as well as in the later months of pregnancy. Experience confirms that penicillin is superior to other treatment methods in the prevention of prenatal syphilis, the failure-rates in terms of syphilitic infants remaining 1%-4% when the mother is adequately diagnosed, treated, and followed during pregnancy. In syphilis in pregnancy, treated at a time when there is no evidence that damage to the foetus has occurred, there is no valid reason to anticipate an unfortunate outcome as regards the infant, although the possibility, however remote, that a post-treatment relapse in the mother could lead to

congenital damage of the foetus, should be envisaged. Some divergence of opinion exists as to the necessity for re-treatment during every subsequent pregnancy of the syphilitic woman. The possibility of the mother being reinfected dictates that every precaution should be taken so as to ensure freedom from the disease in her subsequent children.

Treatment reactions during pregnancy have not proved to be serious and do not usually necessitate any modification of the treatment course. Preparations of PAM now available appear to give satisfactory results with individual doses of 600,000 Oxford units, given once daily, for total courses of 4,800,000 to 6,000,000 units of penicillin. Treatment of the pregnant woman with PAM at 2-3 day intervals is still distinctly experimental. The optimum duration of the treatment course with penicillin for the syphilitic pregnant woman has not yet been determined.

In prenatally acquired syphilis — congenital syphilis in infants — the mortality-rate is high (10%-15%). Great care should be taken with respect to supporting paediatric care during penicillin treatment, as therapeutic shock may be observed. Because of the frequent occurrence of pneumonia and other intercurrent infections, it is considered desirable by some investigators not to modify the penicillin dosage.

It has been common practice to employ aqueous penicillin in early infantile syphilis by frequent injections in hospitalized cases (from 100,000-400,000 units per kg. body-weight, every three hours, for 120 injections). In selected cases PAM has proved satisfactory in individual doses of 150,000 to 300,000 units per injection once daily, although such experience is limited at this time.

Response of serological tests, quantitatively followed, is in direct ratio to the age at which treatment is commenced. When treatment is started under the age of six months, reversal to negativity approaches 100%.

3.2.1.3 *Other public-health aspects.* The advent of PAM has simplified therapy in syphilis and other treponematoses — yaws, pinta, bejel — in which a foreshortened approach has been employed. The development of reliable non-toxic absorption-delaying preparations furnishes an actual and potential epidemiological tool, previously not available; it is effective in severing the chain of infection in treponemal disease in man after initial application of even limited amounts of the antibiotic administered over periods of from hours to a few days. The applicability of this tool to large population-groups represents a major public-health development. Programmes designed to employ this tool on a larger scale should be organized as part of public-health activities in areas with a high prevalence of treponemal disease. These aspects are referred to in section 2.3.

The committee adopted the following resolution :

The Expert Committee on Venereal Infections

Recognizing the epidemiological value of penicillin,

RECOMMENDS

- (1) that penicillin be used for immediate treatment of early infectious, prenatal and infantile syphilis ;
- (2) that procaine penicillin G in oil with 2% aluminium monostearate be used as widely as possible ; and
- (3) that a corresponding group, composed of three members of the committee, report at a subsequent meeting on a review of suitable case-material treated with (a) arsenicals and/or bismuth, and (b) penicillin preparations.

4. SERODIAGNOSIS ²⁴

Any sound venereal-disease activity is dependent to a major degree upon the efficient conduct of serological tests for syphilis. The committee has previously outlined the great lack of uniformity of procedure, technique, and the manner of reporting results which has had the effect of producing confusion and rendering valueless many studies of serology in syphilis and of prevalence of the disease. The problem of biologically false-positive reactions and non-specific reactions in diseases other than syphilis has caused a wide search for further approaches to the problem. The most promising development in this regard is the introduction of the immobilizing antibody technique (Nelson and Turner) ; this has presented an opportunity for studying the wider aspects of immunological relationship between strains of *T. pallidum* and other treponematoses. The differentiation between what appear to be true and non-specific reagins employing this technique may in future prove of fundamental importance in the serodiagnosis of syphilis. Until the scientific evaluation of the merits of this development, now in its early stages, becomes available, the serological programmes must proceed along established lines, the treponemal antibody techniques remaining for the time being entirely a research tool.

The committee has received and studied the report of the Subcommittee on Serology and Laboratory Aspects.²⁵ The committee approves fully the

²⁴ The Executive Board, at its fifth session, adopted the following resolution :

The Executive Board

NOTES the statement of the expert committee on serodiagnosis and laboratory aspects (section 4 of the report).

²⁵ *World Hlth Org. techn. Rep. Ser.* 1950, 14

findings of this group, and the views and recommendations set forth. It agrees that this report be annexed to the report of the main committee, with the following observations :

The determination of the level of reactivity or sensitivity at which standard procedure is to be adjusted in order to convey the soundest information in terms of clinical syphilis is of major significance. This can be established only through the results of broad clinical and laboratory studies. The groundwork for this type of activity is being laid at present in one area, the USA, and similar studies in other parts of the world are necessary. A second consideration is the international exchange of information regarding the prevalence of syphilis based on serodiagnostic findings. This information would be of greater value if a universal test procedure could be employed, although it is recognized that a certain degree of non-specific findings are inescapable with the methods at present used. Should a more reliable and informative standard test-procedure, as well as a standardized antigen based on cardiolipin-lecithin, be introduced on a national scale in one country, this may influence the orientation in other countries. WHO should watch such developments closely with a view to the establishment of an international antigen standard, and the eventual recommendation of a uniform test-method available to all countries where syphilis work is undertaken. This should remain the ultimate aim of WHO in this field. The many confusing factors which are present at this time would then be eliminated.

The disproportionately high percentage of serological findings among inhabitants in certain geographical areas without concomitant proof of syphilitic manifestations remains. The contention is that test methods which are capable of producing a satisfactory standard of results in temperate climates are not equally reliable when applied to population groups under tropical conditions. The impression is gaining strength that the rate of positivity is higher than is to be expected in relation to the frequency with which clinical manifestations of treponemal diseases are encountered ; also, that the presence of other diseases or infestations has not been noted with sufficient frequency to warrant the assumption that they are responsible for the serological phenomenon. This situation may not necessarily constitute an indictment of present-day serology. As the natural history of treponematoses becomes more clearly understood, the possibility of the tests themselves being capable of detecting changes attributed to the presence of syphilis-like organisms may be an eventuality, and may point towards the presence of subclinical treponemal infection which has escaped detection by all other methods. Looking ahead, it will be necessary to gather more precise information on the subject through sampling operations in many tropical areas, including the study of inter-current infections, infestations, and the dietary and living habits of the

population. With its far-flung machinery WHO could contribute substantially to such a study.

The committee recognized the desirability of developing a rapid serological test for ambulatory use in mass-screening procedures sufficiently sensitive and specific for the establishment of diagnosis and the rapid application of therapy during short stays of field units in any one community in less-developed areas with a high prevalence of syphilis. The difficulties in selecting such a test are clear from the foregoing, although various applicable procedures with recognized limitations are in use at this time, e.g., variations of the Chediak "blood-drop" technique, slide tests, filter paper procedures, etc. The committee will watch with considerable interest the work of the Subcommittee on Serology and Laboratory Aspects in this regard.

In approving the report of the first session of the Subcommittee on Serology and Laboratory Aspects, and the recommendations contained therein, the committee adopted the following resolution:

The Expert Committee on Venereal Infections

NOTES with satisfaction the progress made in the formulation of detailed plans for the International Serodiagnostic Laboratory Conference, approved by the World Health Assembly, to be held in a major laboratory centre in 1951 or 1952;

CONSIDERS it important that WHO bring, as soon as possible, the programme outlined for the laboratory conference to the attention of national health-administrations and laboratories, with a view to preliminary registration of participants during the first half of 1950; and

POINTS OUT particularly the desirability of

(1) WHO bringing to the attention of health administrations the necessity for maintaining a national reference laboratory for serodiagnosis of syphilis to control and guide serodiagnostic performances of local laboratories; and of

(2) the subcommittee proceeding as actively as possible with its programme for the establishment of an international antigen reference standard, in close co-operation with the Expert Committee on Biological Standardization, and that the possibility be studied of recommending a uniform test-procedure available to all countries; further that the establishment of international reference centres making available control sera and antigens to national laboratories be explored.

5. CASE-FINDING AND HEALTH EDUCATION

A major effort should be directed towards case-finding in reservoirs of infection which perpetuate transmission of disease in a population group. When control forces actively succeed in reducing incidence and

prevalence of syphilis and related diseases, the relative weight which must be allocated to the finding of the remaining individual cases increases. Available techniques for case-finding should be studied more closely in the light of present information, as well as in relation to characteristics of the particular areas and populations where activities are envisaged.

Available case-finding mechanisms include :

(1) contact investigation, i.e., epidemiological investigation, which is considered to be the most important single approach to finding cases of early syphilis ;

(2) public information and health education, employing a variety of techniques ;

(3) " screening processes ", including prenatal, premarital serological testing, etc., aiming at mass examination of individuals in occupational, economic, or other population groups.

There is evidence in several countries that there is a larger proportion of undiscovered females in the reservoir of venereal infections than there are males. This problem should receive special attention. The entire field of case-finding in syphilis and related diseases, the methods and techniques used, and the adaptation of these techniques to varying environments in different countries merits detailed consideration by the committee at a subsequent meeting.

It is recognized that in many parts of the world there is a great need to develop understanding and knowledge of measures to promote health and to prevent illness. The committee expressed its approval of the definitions, principles, and objectives of the WHO programme in the field of health education. It noted the WHO statement in this regard, and the suggested activities for venereal-disease control. The health education measures and the activities proposed for the WHO venereal-disease teams working with health administrations in the field should be implemented ; such venereal-disease specialists should enter the field and contribute to the development of an informed opinion, with a view to overcoming cultural and social patterns which may hamper health programmes.

The committee wished to emphasize the basic importance of the maintenance of the patient-physician relationship, and the opportunities for the physician to develop a primary understanding in the patient of the nature of venereal diseases, their epidemiology, and the necessity for bringing possible exposed contacts to treatment.

The committee wished to point out the role which non-governmental and voluntary organizations can play internationally, in each country, and in the community in furthering health education programmes.

The committee adopted the following resolution :

The Expert Committee on Venereal Infections

Recognizing the significance of case-finding methods in the control of syphilis and related diseases, and that under the WHO programme advice may be sought by health administrations on available mechanisms, their efficiency, and the applicability of techniques under varying circumstances,

RECOMMENDS that an inquiry into case-finding as applied in venereal-disease control work with special reference to syphilis should be undertaken, and that material be collected from members of the committee, from health educators, and from other sources, as a basis for a report on this subject to be presented to the fourth session of the committee.

6. WHO SYPHILIS STUDY COMMISSION TO THE USA

The committee recalls the activities in the past of the New York Venereal Disease Commission to the Scandinavian countries,²⁶ the special commission appointed by the British Ministry of Health and the Secretary of State for Scotland to report on anti-venereal-disease measures in the Scandinavian countries and Holland,²⁷ and the report of the Anglo-American Caribbean Commission,²⁸ and notes the response of WHO to the original request of the USA Government leading to the establishment of the WHO Syphilis Study Commission. The activities of the commission and the presence of its members during the meeting of the committee have been welcomed. As an effort by WHO to develop international relationships in the technical field of health, the committee observes the favourable outcome of the undertaking.

The committee heard the statement of the chairman of the commission, and holds the view that the report of the commission²⁹ represents a significant contribution which many health administrations, institutions, and workers in venereal-disease will wish to have as a reference document in the future. Valuable information on the US venereal-disease control programme, including data on penicillin in early syphilis and prenatal and infantile syphilis, was collected by the commission and evaluated; this made possible a fuller consideration of this important question during the present session.

²⁶ See *Amer. J. Syph.* 1936, 20, part 2, 7.

²⁷ See *Rep. publ. Hlth Subj., Lond.* 1938, no. 83.

²⁸ Wenger, O. C. (1946) *Caribbean Medical Center*, Washington

²⁹ *World Hlth Org. techn. Rep. Ser.* 1950, 15

The committee adopted the following resolution :

The Expert Committee on Venereal Infections

Considering the establishment of ad hoc study commissions of an international character—by which evaluation of health programmes of special national or international importance may be carried out—to be a valuable technique which WHO may wish to employ at the request of health administrations in the future,

RECOMMENDS that the report of the WHO Syphilis Study Commission to the USA be published early in 1950, and be made available to health administrations and other interested parties.

7. RELATIONSHIPS WITH OTHER INTERNATIONAL ORGANIZATIONS AND WITH COMMITTEES WITHIN THE STRUCTURE OF WHO

The committee notes the co-operation established by WHO in relation to projects and programmes for the combating of venereal diseases, notably with ILO, the International Refugee Organization (IRO), UNICEF, and the International Union against Venereal Diseases, the last-named agency being the only non-governmental international anti-venereal-disease organization with whom WHO has entered into official relationship. Specific reference has been made elsewhere in this report to the projects going forward in co-operation with ILO and UNICEF. As regards the International Union against Venereal Diseases, the committee notes the resolutions of the General Assembly in Rome, and expresses the hope that the Union will continue to study venereal-disease projects having important social significance suitable for international action, and that the activities of the organization will go forward with emphasis on positive health education, and other basic social problems relating to venereal-disease control.

Within the framework of WHO, the committee notes the recommendations made by the Expert Committees on Biological Standardization, Mental Health, and the Unification of Pharmacopoeias, as well as the Joint ILO/WHO Committee on the Hygiene of Seafarers, consideration having been given by the committee to the respective subjects under health education, serology in syphilis, antivenereal drugs, international health regulations, etc. The relationship of the main committee to the Subcommittee on Serology and Laboratory Aspects, and to the WHO Syphilis Study Commission to the USA has been specifically referred to under the respective sections.