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DE LA SANTE

INFORMAL MEETING ON MEASLES  
VACCINE STUDIES

**INDEXED**

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[ REPORT ]



Participants

- Dr J. F. Enders, The Children's Hospital, 300 Longwood Avenue, Boston 15, Massachusetts, United States of America
- Dr J. H. S. Gear, Director, The South African Institute for Medical Research, P.O. Box 1038, Johannesburg, South Africa (Chairman)
- Dr M. R. Hilleman, Director, Merck Institute for Therapeutic Research, West Point, Pennsylvania, United States of America
- Dr C. H. Kempe, Department of Paediatrics, University of Colorado Medical Center, 4200 East Ninth Avenue, Denver 20, Colorado, United States of America
- Dr N. L. de Araujo Moraes, Fundacao Servico Especial de Souda Publica, Rio de Janeiro, Brazil
- Dr Y. Okuno, The Research Institute for Microbial Diseases, Osaka, Japan
- Dr J. R. Paul, Department of Epidemiology and Public Health, Yale University School of Medicine, 333 Cedar Street, New Haven 11, Connecticut, United States of America
- Dr A. M.-M. Payne, Chairman, Department of Epidemiology and Public Health, Yale University School of Medicine, 310 Cedar Street, New Haven 11, Connecticut, United States of America
- Dr C. Ristori, Servicio Nacional de Salud, Santiago, Chile
- Dr L. Rosen, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda 14, Maryland, United States of America
- Dr V. M. Zhdanov, Academic Secretary, Academy of Medical Sciences of the USSR, Solyanka 14, Moscow, USSR

Secretariat

Dr W. Charles Cockburn, Chief Medical Officer, Virus Diseases, Division of Communicable Diseases, WHO/HQ

Dr A. N. Bica, Branch Chief, Communicable Diseases, Pan American Sanitary Bureau

Dr A. Vilches, Regional Adviser, Endemo-epidemic Diseases, Regional Office for the Americas

1. Introduction

On 10 November 1961 a meeting was held at the Regional Office of the World Health Organization for the Americas to discuss the role of WHO in the epidemiology of measles with special reference to immunization against the disease in developing countries with high mortality rates. The participants were drawn from members of an International Conference on Measles Immunization sponsored by the Department of Paediatrics, University of Colorado School of Medicine and held at the National Institutes of Health, Bethesda, Maryland, on 7 to 9 November.

The agenda (Annex 1) was adopted and Dr J. H. S. Gear was elected Chairman.

2. The role of WHO in epidemiological and vaccine studies

The role of WHO in epidemiological and vaccine studies was described by the Secretariat. Dr Payne stressed its function in planning field studies and in proposing standard methods of procedure to ensure comparability of results from studies made in different areas or at different times.

3. Epidemiological studies on measles

The information presented at the International Conference on the Incidence and Mortality of Measles in Different Countries was reviewed and noted. Its value was appreciated, but it was recognized that in many areas where mortality from the disease was high, detailed epidemiological data were lacking. Though the development of measles vaccines and their successful use had progressed rapidly in recent months, more extensive and accurate data were urgently required.

RECOMMENDATION: It was therefore recommended that WHO should:

- (1) Collate and disseminate to those interested the available information from the reports given at the recent International Congress, the health authorities in countries with high mortality rates, the South Pacific Commission, and other similar sources.
- (2) Encourage, support and co-ordinate special surveys in areas of high mortality, for example India, Nigeria, Gambia, Upper Volta, Chile and Brazil, to determine the age incidence of infection and the time intervals between epidemics; to define the clinical picture accurately; and to investigate the fundamental causes of high death rates. These detailed surveys were essential as the information obtained under (1) would be incomplete.
- (3) Encourage, support and co-ordinate surveys in areas which had been free of infection for long periods and in which both adults and children were at special risk. In these areas sera from all age-groups should be obtained. Examination of the sera would present few technical difficulties but it was recognized that many of the areas were remote and the collection of the sera presented considerable problems. WHO should therefore obtain information, for example by correspondence with members of the Expert Panel, on serological surveys (not only in connexion with measles) which were contemplated or being carried out so that samples for examination for measles antibody could be obtained. It was mentioned that serum surveys were being made in the Pacific Islands and that some of the sera might be made available to WHO. The Serum Reference Banks should collaborate in these studies. The surveys would provide information on areas where trials of measles vaccines in adults could be set up. In addition, when acceptable effective vaccines become freely available, knowledge of areas of special risk would be of value in ensuring rapid distribution of vaccine if infection was introduced.

Standard methods for the performance of serological tests were essential before reliable comparisons between areas could be made. Dr M. Hilleman agreed to provide details of a recommended method. Standard sera and strains of virus were held by Dr Dorland Davis, Associate Director in Charge of Research, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland, and it was recommended that he be asked to provide sera and strains for the serological studies.

4. Studies of measles vaccine

Four different vaccines had been described at the International Conference.

They were:

- (a) vaccine prepared from the Edmonston B strain (Dr Enders) and given with or without gamma globulin. Dr Smorodintsev had prepared a vaccine of this type;
- (b) vaccine prepared from a further-attenuated strain, substrain of the Edmonston and described by Dr Schwartz;
- (c) vaccine prepared from an attenuated strain described by Dr Faydeeva;
- (d) inactivated vaccines.

The different properties of the vaccines were discussed and the setting up of studies in areas of high mortality was considered. The "Schwartz vaccine" was promising because it caused less reaction than the Edmonston strain vaccine, but it was still at a very early stage of development and was unlikely to be immediately available for trial.

The extensive use of inactivated vaccine would only be justified by mixing it with other antigens. It was important that it should be studied further. Information on the production of antibody when it was mixed with other antigens, which should be the first objective, could be obtained quickly in countries where adequate laboratory facilities were readily available and studies should therefore be set up in these countries before tests were made in developing countries.

Dr Faydeeva's vaccine was at present undergoing trial in the USSR.

CONCLUSION: It was concluded that in the immediate future only vaccine prepared from the Edmonston strain would be available for trial in developing countries.

RECOMMENDATION: It was recommended that WHO should encourage, support and co-ordinate trials with the vaccine without delay.

In the first place the trials should be made on a small scale in a number of different countries simultaneously in accordance with a uniform plan. The object was two-fold:

- (a) to determine the severity of vaccine-induced illness when vaccine was administered alone and with varying doses of gamma globulin;
- (b) to measure antibody responses.

At Dr Enders' request, Dr M. Hilleman agreed to supply vaccine and gamma globulin for the trials. The same batch of vaccine and of gamma globulin would be used in all areas.

Dr Cockburn agreed to prepare a plan of the study in collaboration with the Division of Health Statistics for consideration by the participants.

In each trial vaccines should be administered according to the following schedules:

- A. Vaccine alone
- B. Vaccine + 0.01 ml gamma globulin per lb. body weight
- C. Vaccine + 0.005 ml gamma globulin per lb. body weight
- D. Vaccine + 0.0025 ml gamma globulin per lb. body weight
- E. Placebo

The vaccine would be injected subcutaneously into one arm and the gamma globulin into the other at the same time.

The placebo injection would consist of a killed measles vaccine.

In each area 50 children between six months and three years of age should be included in each vaccine group. This would give a total of 250 children. (After consultation with Dr Hilleman subsequent to the meeting it is suggested that the numbers in each trial should be increased to 500 as some of the children in the age-group to be tested may already be immune as a result of natural infection. Dr Hilleman is prepared to supply vaccine and gamma globulin for the larger numbers - W. Chas. Cockburn)

The following participants agreed to collaborate: Dr N. L. Moraes, Brazil; Dr C. Ristori, Chile; Dr Y. Okuno, Japan; Dr C. H. Kempe (study in Madras); Dr J. H. S. Gear, South Africa; Dr V. Zhdanov, USSR.

In addition, Dr MacGregor, Gambia and Dr Montefiore, Nigeria, should be invited to co-operate.

(Since the meeting Dr Djukanovic, Yugoslavia, has asked to participate - W. Chas. Cockburn)

The validity of the results of the serological tests would be enhanced if they could be carried out in one laboratory rather than in a number of different laboratories and it was recommended that the World Health Organization should explore the possibility of finding a laboratory with adequate facilities for this purpose.

It was recognized that in due course other vaccines would become available for trial and that further studies on the lines indicated above would then have to be considered.

5. Other business

There was no other business.

DRAFT AGENDA

1. Appointment of Chairman
2. The role of WHO in epidemiological and vaccine studies
3. Participation of WHO in epidemiological studies on measles
  - (a) Problems needing answers
4. Participation of WHO in studies on measles vaccine
  - (a) Problems needing answers
  - (b) Future of measles vaccines in different areas of the world
5. Other business