WORLD HEALTH ORGANIZATION

REGIONAL OFFICE FOR THE WESTERN PACIFIC

REPORT

MEETING OF THE TASK FORCE ON HEPATITIS B

Manila, Philippines
8-11 November 1983

Manila, Philippines
March 1984

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REPORT

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Sponsored by the

WORLD HEALTH ORGANIZATION REGIONAL OFFICE FOR THE WESTERN PACIFIC
Manila, Philippines

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Manila, Philippines

March 1984

NOTE

The views expressed in this report are those of the Members of the Task Force and do not necessarily reflect the policies of the Organization.

This report has been prepared by the Regional Office for the Western Pacific of the World Health Organization for governments of Member States in the Region and for those who participated in the Meeting of the Task Force on Hepatitis B, which was held in Manila, Philippines from 8 to 11 November 1983.

CONTENTS

1. INTRODUCTION

Hepatitis B infection is one of the major public health problems in the Region. In most countries, the disease is hyperendemic and from 5-15% of the population are persistent carriers of the virus. It is estimated that there are approximately 160 million carriers of Hepatitis B virus (HBV) in the Western Pacific Region and that up to 40% of these will ultimately die from the long-term sequelae of chronic infection, namely, chronic liver disease or liver cancer.

In the past few years, safe effective vaccines have become available and have been licensed in many countries. Providing support to Member States in the mass production and administration of hepatitis B vaccine should have a high priority in WHO's programme.

Liver cancer is one of the three most common cancers in the Region so that the availability of a vaccine provides a unique opportunity to prevent a major cancer by vaccination.

It is recognized that control of hepatitis B infection and its sequelae is an interdisciplinary activity requiring the participation of clinicians, virologists, immunologists, epidemiologists, oncologists and public health administrators. The delivery of hepatitis B vaccine should be coordinated with the Expanded Programme on Immunization (EPI) with the aim of eventual integration with the programme.

2. BACKGROUND AND OBJECTIVES

The Scientific Group on Hepatitis B Virus and Its Related Virus Diseases, at its meeting from 29 September to 2 October 1982, in Nagasaki, Japan, recommended that a small regional task force should be convened on an ad hoc basis consisting of representatives of institutions with special expertise in the field of viral hepatitis.

Pursuant to this recommendation, the WHO Regional Office for the Western Pacific established a Task Force on Hepatitis B with the following objectives:

To act as a coordinating body for WHO's regional programme on hepatitis by:

- collecting and analysing data;
- defining areas which require further research and assisting in the the development of collaborative research proposals;

- closely reviewing progress in vaccine development and its application in the Region, especially in preventing maternal/infant transmission;

- coordinating research in the Region;

- encouraging the sharing of data and the effective use of resources.

It was decided to hold the present meeting with the following objectives:

(1) to define areas which require further research;

(2) to review progress in vaccine development and its application in the Region; and

(3) to review other data on intervention studies and to advise the Regional Director of the WHO Regional Office for the Western Pacific on the need for additional studies.

Furthermore, it was felt timely and necessary to discuss the following aspects of hepatitis B vaccines: production capabilities, product quality, quality control, stability and certification of the finished product, the labelling of preparations and their distribution.

3. SUMMARY OF PROCEEDINGS

The meeting was opened by the Regional Director, Dr Nakajima. Dr Nishioka was nominated as Chairman of the Task Force, Dr Li Ho Min as Vice Chairman, and Dr Gust as Rapporteur.

The Group discussed the current status of production of hepatitis B vaccines in the Region. Plasma-derived particle vaccines are currently being produced in Japan by three commercial manufacturers, in the Republic of Korea and in China. In addition, Singapore has signed an agreement with Merck Sharp and Dohme which will result in the local production of vaccine within the next two years. Other countries in the Region continue to rely on vaccine imported from overseas.

A variety of studies with the currently licensed French and American vaccines have been performed in the Region and further studies with local vaccines are in progress or being planned. Considerable variations exist in the manufacturing processes selected, the degree of expertise of the staff involved in production and the quality control procedures which are carried out by the manufacturers and national control authorities.

Studies on the purity, potency and efficacy of the local vaccines are in progress. There is no consensus yet as to the optimal dose of vaccine or immunization schedule, although it is widely accepted that administration of the vaccine should fit into the Expanded Programme on Immunization.

Some countries have begun to produce their own diagnostic reagents but the quality of these is widely variable. The group discussed the choice of test systems and mechanisms by which WHO could assist in the production, distribution and quality control of sensitive, low-cost reagents.

Finally the Task Force considered the strategies for immunization and target groups which should receive priority in the Region. It was felt that, while limited supplies of vaccine would force most countries to restrict immunization to high-risk groups for some years, the ultimate aim in most countries of this Region was universal immunization of newborn babies.

4. RECOMMENDATIONS

4.1 Diagnostic reagents

4.1.1 Adequate supplies of reagents for the detection of markers of HBV infection are urgently required to enable countries in the Region:

(i) to study the natural history of the disease, in particular, the time at which infections are acquired, the groups in which infection is most common and the frequency with which perinatal transmission of infection occurs;

(ii) to screen blood donors and population groups for whom vaccine is intended;

(iii) to evaluate the efficacy of immunization programmes.

4.1.2 The test chosen should be sensitive, specific, simple and cheap and be capable of being performed by laboratory workers with limited training and facilities. While the most widely used test is the enzyme-linked immunosorbent assay, other tests of similar sensitivity and specificity, such as reverse passive haemagglutination, are acceptable.

4.1.3 WHO should support collaborating centres in the Region in developing programmes for the production and standardization of diagnostic reagents. The training programmes which are used should be based on, or complementary, to those produced by the WHO Collaborating Centre for Viral Hepatitis at CDC/Atlanta.

4.1.4 The quality of reagents produced by the national or regional laboratories should be checked by collaborative studies organized through a network of collaborating centres and a regional pool of standardized working reagents should be established.

4.1.5 Where countries, through size or lack of technical capability, are unable to produce their own reagents, WHO should attempt to supply them with working reagents.

4.1.6 WHO should collaborate in training personnel who will be capable of producing diagnostic reagents in their own country and training their own support staff. Such courses should be held either in a WHO collaborating centre or in a suitable laboratory in the particular country.

4.1.7 WHO should collaborate in the design and development of quality control programmes and national proficiency testing panels to ensure that testing procedures in each country are maintained at a high level. A consultative mechanism should be developed to assist countries or laboratories which fail to achieve the required standards of performance.

4.2 Hepatitis B vaccine production and control

In most countries of the Western Pacific Region, hepatitis B infection is acquired early in life. Early immunization will therefore be the method of choice for prevention of the carrier state and its long-term sequelae, chronic liver disease and primary liver cell carcinoma.

There is therefore an urgent need for hepatitis B vaccine to be available in large quantities and at a price countries can afford.

4.2.1 Towards this end, through its technical cooperation programmes, WHO should actively support the transfer of technology for production and control of plasma-derived hepatitis B vaccine to countries in the Region with the capability of producing their own vaccine.

4.2.2 WHO should revise the recently proposed requirements for hepatitis B vaccines so as to provide support to countries in the Region which are attempting to produce safe and potent vaccines but do not have access to chimpanzees. Alternative measures to the chimpanzee safety tests should be introduced.

4.2.3 Studies carried out in the Region to date suggest that administration of HBIg and HB vaccine to newborn babies provides more effective protection against infection than active immunization alone. In anticipation that HBIg may be required in addition to vaccine to prevent perinatal transmission of infection, highly potent and low-cost HBIg should be supplied for protection of perinatal infection where indicated.

4.2.4 WHO standard preparations should be made available to competent laboratories in the Region.

4.2.5 While it is recognized that plasma-derived vaccines will be the only vaccines available for several years, WHO should support collaborative research on DNA cloned vaccine or the chemically synthesized peptide vaccine.

4.2.6 Efforts should be made to enhance the heat stability of the vaccine for use in tropical countries. Further studies on lyophilization of vaccine should be carried out.

4.2.7 WHO should actively support the development or strengthening of national vaccine control authorities.

4.3 Immunization strategies

4.3.1 Several studies have been carried out or are in progress to define the optimum dose and immunization schedule for prevention of perinatal transmission of HBV. WHO should gather the available information, submit it to detailed analysis and transmit the results to Member States.

4.3.2 (a) In countries planning immunization programmes where information is not available, WHO should support small-scale field studies to determine optimal dosage and scheduling of hepatitis B vaccine, and to assess the need for combined administration of HBIg and vaccine.

(b) Recognizing that large-scale immunization of infants may be the most effective method of preventing the HBV carrier state in some countries, efforts should be focused on achieving optimum HBV vaccination schedules and the possibility of integration into current EPI programmes.

4.3.3 Recognizing that hepatitis B vaccine is the most important preventive measure for primary liver cancer, WHO should encourage the initiation of demonstration vaccination field trials in one or more countries of the Region where the prevalence of the HBV carrier state and of hepatocellular carcinoma is high. These trials should be designed to evaluate the effect of immunization on the prevalence of HBV carrier state in successive cohorts of children as well as to allow evaluation of the effect of hepatocellular carcinoma mortality several years in the future. The host countries should seek the support of the WHO Western Pacific Region Task Force on Hepatitis B in the design and monitoring of these field projects.

4.4 Technical cooperation

WHO should encourage the strengthening of manpower for the production of vaccines and diagnostic reagents and the conduct of diagnostic test such as by providing fellowships and consultant services. WHO should also endeavour to standardize, coordinate and implement field studies on epidemiological surveillance and efficacy of vaccines.

4.5 Task Force

The group recommended that the Regional Director should establish the Task Force on a formal basis.

It is suggested that future meetings of the Task Force be held in countries of the Region in which active control programmes are in progress and are being developed, so that members of the Task Force could provide expert advice to local workers.

ANNEX 1

LIST OF MEMBERS, TEMPORARY ADVISERS, OBSERVERS AND SECRETARIAT

1. MEMBERS

AUSTRALIA	Dr I.D. Gust Director Virus Laboratory Fairfield Hospital Yarra Bend Road Fairfield, Victoria 3078
CHINA	Dr Duan Shucheng Deputy Director Children's Hospital First Medical College of Shanghai Shanghai
	Dr Li Ho-min Director National Institute for the Control of Pharmaceutical and Biological Products Temple of Heaven Beijing
JAPAN	Dr K. Nishioka Vice President Tokyo Metropolitan Institute of Medical Science Tokyo 113
	Dr Mitchitami Yano Director WHO Collaborating Centre for Reference and Research on Viral Hepatitis National Nagasaki Central Hospital Kubarago 603-1 Omura City 836 Nagasaki

ANNEX 1

1. MEMBERS (cont'd.)

PHILIPPINES	Dr E. Domingo Team Leader Liver Study Group Department of Medicine Philippine General Hospital Taft Avenue Manila
REPUBLIC OF KOREA	Dr Whan Kook Chung Professor of Internal Medicine Director, St Mary's Hospital Catholic Medical School 2Ka-1, Myungdong, Junggu Seoul
SINGAPORE	Dr Goh Kee Tai Head, Quarantine and Epidemiology Unit Ministry of the Environment Singapore 0315
UNITED STATES OF AMERICA	Dr J. Maynard Director WHO Collaborating Centre for Hepatitis Reference and Research Centers for Disease Control Atlanta, Georgia 30333

2. TEMPORARY ADVISERS

CHINA	Dr Zhao Kai Chief, Department of Hepatitis National Vaccine and Serum Institute Beijing
	Dr Shen Yan Chief, Division of Biological Products Ministry of Public Health Beijing

ANNEX 1

2. TEMPORARY ADVISERS (cont'd.)

Dr Tao Yi-Xun
Vice-Director
Shanghai Medical Laboratory
3/120 Tai An Road
Shanghai 200031

Professor He Baoguang
Head
Laboratory for Research
on Cell Biology
Shanghai Institute
of Biological Products
Shanghai

JAPAN

Dr H. Shimojo
Director
Department of Enteroviruses
National Institute of Health
Kamiosaki, Shinagawa-ku
Tokyo 141

Dr N. Ohtomo
Director of Research and Development
The Chemo-Sero-Therapeutic
Research Institute
668 Okubo Shimizu
Kumamoto 860

Dr T. Takahashi
Head of Hepatitis Research Unit
The Kitasato Institute
5-9-1 Shirokane, Minato-ku
Tokyo 108

Dr M. Nishida
Managing Director
Central Research Laboratories
The Green Cross Corporation
1-15-1 Imabashi, Higashi-ku
Osaka 541

ANNEX 1

2. TEMPORARY ADVISERS (cont'd.)

REPUBLIC OF KOREA

Dr K.H. Kim
Director
Central Research Laboratory
Korea Green Cross Corporation
D.P.O. Box No. 8
Seoul (S)

Dr Jung Han Park
Associate Professor
Kyungpook National University
School of Public Health
101 Dong In Dong
Taegu

3. OBSERVERS

Dr Y. Kaneko
Team Leader/Expert
Japan International Cooperation Agency
Research Institute
for Tropical Medicine
Alabang
Metro Manila

Dr A. Lingao
Liver Study Group
Philippine Center for
Health Sciences
Philippine General Hospital
Taft Avenue
Manila

4. SECRETARIAT

Dr F. Assaad
Director
Division of Communicable Diseases
WHO Headquarters
Geneva

ANNEX 1

4. SECRETARIAT (cont'd.)

Dr I. Geizer
Acting Director
Disease Prevention and Control
WHO Regional Office for the
Western Pacific
Manila

Dr Y.H. Paik
Chief, Research Promotion
and Development
WHO Regional Office for the
Western Pacific
Manila

Dr J. Stjernswärd
Chief, Cancer Unit
WHO Headquarters
CH1211, Geneva 27

Dr T. Umenai
Regional Adviser
in Communicable Diseases
WHO Regional Office for the
Western Pacific
Manila

ANNEX 2

AGENDA

Tuesday, 8 November

0830	Registration	
0900	Opening Ceremony	Dr Nakajima
	Adoption of Agenda	
	I. Production of Hepatitis B Virus Vaccines	
0915	Japan	Dr H. Shimojo Dr T. Takahashi Dr N. Ohtomo
1015	Coffee break	
1030	Japan	Dr M. Nishida
	People's Republic of China	Dr Li Ho Min Dr He Baoguang Dr Shen Yan
1200	Lunch break	
1330	Republic of Korea	Dr K.H. Kim
	Singapore	Dr Goh Kee Tai
1500	Coffee break	
1515	II. Rehearsal for Hepatitis B Symposium	
1650	III. Review of progress in intervention study - general view	Dr M. Yano

ANNEX 2

AGENDA (cont'd.)

Wednesday, 9 November

	IV. Quality of diagnostic reagents being produced of used	
0830	Japan	Dr M. Mayumi
	People's Republic of China	Dr Tao Yi-Xun
	Australia	Dr I.D. Gust
	Republic of Korea	Dr K.H. Kim
0945	Coffee break	
	V. Quality of hepatitis B vaccines produced or being used	
1000	Japan	Dr H. Shimojo
	People's Republic of CHina	Dr Li Ho-Min
	Republic of Korea	Dr W. K. Chung
1130	Lunch break	
1330	VI. Hepatitis B Symposium in International Paediatric Congress	

Thursday, 10 November

	V. Quality of hepatitis B vaccine being produced or used	
0830	Singapore	Dr Goh Kee Tai
	Australia	Dr I.D. Gust
0945	Coffee break	

ANNEX 2

AGENDA (cont'd.)

	VII. Quality control and national safety criteria for hepatitis B vaccines	
1045	Global view	Dr F. Assaad
	Regional view	Dr K. Nishioka
	Discussion	
1200	Lunch break	
	VII. Quality control and national safety criteria for hepatitis B vaccines	
1300	Discussion	
1500	Coffee break	
	VIII. Vaccination and targets of vaccines	
1515	General view	Dr K. Nishioka
	Discussion	

Friday, 11 November

0830	Drafting of recommendations
1000	Coffee break
1015	Drafting of recommendations (cont'd.)
1200	Lunch break
1330	Finalization of recommendations
1500	Closing ceremony