



WORLD HEALTH ORGANIZATION
ORGANISATION MONDIALE DE LA SANTE

38517

DISTR. : LIMITED
DISTR. : LIMITEE

WHO/MIM/VDT/91.457
ORIGINAL: ENGLISH

CONSULTATION ON HEPATITIS B AS A
SEXUALLY TRANSMITTED DISEASE

Report of a WHO Consultation
Geneva, 28-30 November 1990

Microbiology and Immunology Support Services
Programme of Sexually Transmitted Diseases

This document is not issued to the general public, and all rights are reserved by the World Health Organization (WHO). The document may not be reviewed, abstracted, quoted, reproduced or translated, in part or in whole, without the prior written permission of WHO. No part of this document may be stored in a retrieval system or transmitted in any form or by any means - electronic, mechanical or other - without the prior written permission of WHO.

The views expressed in documents by named authors are solely the responsibility of those authors.

Ce document n'est pas destiné à être distribué au grand public et tous les droits y afférents sont réservés par l'Organisation mondiale de la Santé (OMS). Il ne peut être commenté, résumé, cité, reproduit ou traduit, partiellement ou en totalité, sans une autorisation préalable écrite de l'OMS. Aucune partie ne doit être chargée dans un système de recherche documentaire ou diffusée sous quelque forme ou par quelque moyen que ce soit - électronique, mécanique, ou autre - sans une autorisation préalable écrite de l'OMS.

Les opinions exprimées dans les documents par des auteurs cités nommément n'engagent que lesdits auteurs.

TABLE OF CONTENTS

	Page
1. INTRODUCTION	3
2. CONSENSUS STATEMENT	3
2.1. Epidemiology	3
2.2. Consequences of HBV infection in adults	4
2.3. Prevention and Control	5
2.3.1. Pre-exposure prophylaxis	5
3. RECOMMENDATIONS	7
3.1. Prevention strategies	7
3.1.1. Risk behaviour reduction	7
3.1.2. Immunization policies	7
3.1.2.1. Policies in areas of high and intermediate endemicity	8
3.1.2.2. Policies in areas of low endemicity	8
3.1.3. Optimum patient care	8
4. RECOMMENDATIONS FOR RESEARCH IN THE AREA OF HEPATITIS B AS A SEXUALLY TRANSMITTED DISEASE	9
4.1. Natural history and transmission	9
4.2. Epidemiology	9
4.3. Operational issues	9
4.4. Cost effectiveness	10
5. LIST OF PARTICIPANTS	11

1. INTRODUCTION

A consultation on hepatitis B as a sexually transmitted disease (STD) was convened by the World Health Organization's Microbiology and Immunology Support Services, and the Sexually Transmitted Diseases Programme, from 28-30 November 1990, in Geneva, Switzerland. A total of 11 participants from 8 countries participated, including experts in public health, epidemiology, virology and biomedical aspects of hepatitis B virus and other STD.

Hepatitis B is one of the major diseases of mankind, with severe consequences in terms of morbidity, mortality, and economic impact. Long term control of this disease is now feasible with a safe and effective vaccine, and issues related to its control should now be seriously considered by public health authorities. Hepatitis B virus (HBV) infection is the first vaccine-preventable sexually transmitted infection (STI), and serves as a model for use of vaccines in future STD prevention programmes.

It has been known since the early 1970's that hepatitis B is an important sexually transmitted disease. In some countries in North America, Latin America, and Europe, sexual transmission is the major identified mode of HBV transmission. The role of sexual transmission in areas of higher HBV prevalence has been less well studied, but sexual transmission plays a significant role in adult transmission in those areas as well.

Despite the fact that the epidemiology of hepatitis B as an STD has been studied for many years, health departments, STD clinics and medical practitioners have often not included this disease and its prevention as one of their responsibilities. HBV vaccine has been available since 1982 and recommendations for its use in STD settings have been made since that time, but little vaccine has been used for this purpose.

The Consultation had the following objectives:

- (1) Review the current state of knowledge about sexual transmission of HBV;
- (2) Develop a consensus statement on guidelines for prevention of sexual transmission of HBV;
- (3) Identify needs and opportunities for research on the epidemiology and prevention of sexual transmission of HBV.

2. CONSENSUS STATEMENT

2.1 Epidemiology

Numerous studies from many parts of the world have documented hepatitis B virus (HBV) infection as an important sexually transmitted disease in both developed and less developed countries. In HBV prevalence studies, groups such as homosexual males, prostitutes (both male and female), and sexual

contacts of HBV carriers and acute HBV cases have invariably been shown to be at highly elevated risk of infection. In developed countries, heterosexual attendees of STD clinics and persons with multiple sex partners or with a history of previous STD have also been at somewhat elevated risk.

In developed countries, the importance of sexual HBV transmission may be variable. In the United States, sexual contact is the most important mode of disease transmission, accounting for over 35% of all infections and 50% of cases with identified risk factors; in recent years, heterosexual transmission has increased in importance while homosexual transmission has decreased. These data, combined with the relatively high incidence of acute hepatitis B (10 cases/100,000/year) and chronic liver diseases (estimated 3000 deaths/year) due to adult infection have stimulated interest in aggressive disease control programmes. In Northern Europe, disease incidence is lower and the importance of heterosexual disease transmission is less well defined; thus, prevention of sexually transmitted HBV infection has been given lower priority. In Southern European countries such as Greece and Italy, HBV prevalence is decreasing due to diminished horizontal transmission among children; in these areas, adult infection is becoming more prominent and heterosexual contact accounts for a substantial proportion of acute hepatitis B cases in adults.

In developing countries, sexual transmission also has variable importance. In Southern Asia, 40-60% of adults are susceptible to HBV infection, and half of these acquire infection in adulthood, many likely due to sexual contact. Prostitutes are at high risk of infection, and where sex with prostitutes is the major source of transmission of STD, this may account for a high proportion of adult HBV infections. In developing countries, fewer adults are susceptible to HBV infection, although those that are, are highly likely to be exposed to HBV carriers. Finally, in the Middle East, where STD may be less common, sexual transmission of HBV infection appears to be relatively unimportant. In contrast, travellers and military personnel from developed countries are at high risk of HBV infection if they have sexual contact with the local population while visiting less developed countries endemic for HBV infection.

The importance of a core group of highly sexually active persons in maintaining sexual transmission of HBV, as occurs with some other STD, has not been well defined. Prostitutes may play such a role in HBV transmission in Asia, and mathematical modelling suggests that such persons may be important in transmission among heterosexuals, but less important among homosexual men, in developed countries. Efforts which successfully target the first two groups therefore may have been disproportionate impact in disease control programmes.

2.2 Consequences of HBV Infection in Adults

While the acute consequences of HBV infection in adults are well defined, and include clinical hepatitis in 25-33% and fulminant hepatitis in 1-2 per 1000 infections, the long-term outcomes have been less well quantitated or communicated to the medical community and public. Prospective studies indicate that 6-7% of infected homosexual men without HIV infection, and 0-10% (mean 7%) of other adults (such as Alaskan natives and blood-transmitted cases) become HBV carriers. Prospective studies indicate that such persons have

15-40 fold increased risk of developing chronic liver disease and primary liver cancer, and estimates from the United States indicate that between 3 and 15% of such persons may eventually die due to these causes. The risk of developing HBV carriage following heterosexual disease acquisition has not been well defined and is worthy of study.

Prior HIV infection has several effects that might increase risk of sexual transmission of HBV infection. HBV infection in HIV-infected persons is more likely to lead to chronic HBV carriage and to higher sustained infectivity to others, although it also results in less active liver disease. HIV infection may also promote reactivation of latent HBV infection, and causes poorer response to hepatitis B vaccine.

2.3 Prevention and Control

Prevention of sexually transmitted HBV infection has been inhibited by inadequate education of the public, of physicians, and of STD specialists that HBV is an STD of importance comparable to or higher than syphilis in both developed and less developed countries. Programmes to educate these groups about the epidemiology and consequences of HBV infection must be of highest priority for all such groups, as should be the incorporation of HBV-specific prevention and control measures into all aspects of standard STD prevention guidelines.

The efficacy of postexposure prophylaxis for sexual contacts of both acute HBV cases and chronic HBV carriers has been well demonstrated; HB vaccine or HBIG alone appear to have about 70-80% effectiveness in preventing clinical hepatitis if given within two weeks of exposure, while combined HB vaccine and HBIG treatment may improve protection to 85-90%.

Recent unpublished research with mathematical modeling suggests that vaccination of a subset of heterosexuals with many sexual partners may have a substantial impact in preventing heterosexual transmission. Identification and access to such individuals, and compliance with the standard six month vaccination regimen may be difficult in many settings. On the other hand, access to core groups of high frequency sexual transmitters of HBV may be feasible in other settings - e.g. where health care programmes have been organized for prostitutes and homosexual men.

2.3.1. Pre-exposure prophylaxis

HB vaccine became available in 1982, and recommendations for its use have been issued by public health groups in many countries. These recommendations note the difference in the epidemiology of HBV infection in areas of different HBV prevalence, and strategies for control vary accordingly. Routine infant immunization with HB vaccine as a part of the Expanded Programme on Immunization (EPI) is recommended for countries with high or intermediate levels of HBV endemicity (HBV carrier prevalence of 2% or greater), while immunization of "high risk" groups and post exposure prophylaxis is recommended for countries of lower endemicity. These "high risk" groups invariably include homosexually active males, prostitutes, and sexual partners of HBV carriers. Some countries also recommend HB immunization of heterosexuals with multiple partners and those attending STD clinics.

The need for targetted immunization to prevent sexually transmitted infection in countries with moderate to high HBV endemicity should be considered only after implementation of universal vaccination of infants. Such countries will need to examine the importance of horizontal transmission among young children and patterns of transmission among adults in making such decisions. Where possible, decisions for programmes should take into consideration the relative cost-effectiveness of various approaches; recently a number of investigators have developed models which may be helpful. If prevention programmes are to be initiated, both targetted vaccination and universal vaccination of adolescents or young adults should be considered. Targetted programmes (e.g. to prostitutes) may be more cost-effective if the target group(s) accounts for a high proportion of cases and if most of this population can be effectively reached with the full vaccine series. Mass vaccination may be preferable if multiple risk groups exist and if some (or all) of these cannot be effectively reached by the programme.

In developed countries the vaccination of high risk groups including intravenous drug users, homosexual men, and those who acquire disease by heterosexual contact has been recommended since vaccine licensure but has had little or no impact on disease incidence in these groups or in the countries as a whole. Major impediments have included high cost of vaccine, failure to obtain resources to sustain programmes, difficulty in identifying and reaching members of these populations while still susceptible, poor compliance in seeking vaccination and in completing the recommended series in highest risk groups, and difficulties in targetting the highest risk heterosexual populations. Modification of the vaccination schedule - to give the final dose two months rather than six months after the first dose - should be considered in STD clinic settings to improve compliance with minimal decreases in seroconversion rates. In addition, development of single dose vaccines would facilitate programmes to prevent HBV infection in adults.

Alternatives to targetted immunization in these areas include routine immunization of infants as part of childhood vaccination programmes, and routine vaccination of adolescents prior to initiation of sexual activity. Routine immunization of infants, in combination with other childhood vaccines, has the advantage of assuring vaccine delivery to a high proportion of the population, but will not appreciably impact on adult disease burden for two decades. Furthermore, depending on the duration of protection by vaccine, one or more booster doses may be necessary later in adolescence or adulthood. Development of multiantigen vaccines (e.g. DTP + HBV) would assure easy implementation of such programmes.

Immunization of all children in early adolescence, before they have begun regular sexual activity, could result in dramatic decreases in sexually transmitted HBV infection within one decade, but may be more difficult to implement successfully than infant immunization programmes. Multiantigen vaccines would be of limited importance in this situation.

Decisions regarding vaccination strategies should take into consideration the relative cost-effectiveness of these various approaches; the increasing interest and development of model analyses for HBV prevention should facilitate such analyses. Epidemiologic data regarding the relative risks of

sexual HBV transmission, and the incidence, disease burden and relative importance of sexual transmission among adults are critical for such analyses; where these data are not available, epidemiologic studies should be initiated to generate them.

3. RECOMMENDATIONS

The consultation made the following recommendations, mindful of the low level of awareness of members of the health care services and the general public of the sexual transmission of HBV infection.

3.1 Prevention Strategies

3.1.1 Risk-behaviour reduction

- (a) The importance of HBV as a sexually transmitted infection should be clearly stated by WHO and national health authorities and included in health education programmes for general public and for special target groups such as male and female sex workers (prostitutes), homosexual and bisexual men, injecting drug users, and health care workers according to local circumstances. HBV prevention should be coordinated with AIDS/STD health education programmes.
- (b) Informed counselling should be available to patients found to have acute or chronic HBV infection to allay anxiety, promote personal health and reduce the risk of further transmission of infection, by promoting safer sexual practices including condom use. Contacts of cases should be sought, counselled and offered screening and immunization as appropriate (see below).
- (c) The risk behaviour reduction strategies remain important because, directed as they are to sexually active groups, benefit may be obtained rapidly. They are the only methods available to control infection among those who are already infected, those for whom vaccine is not available and those who are non-compliant or unresponsive to vaccination.

3.1.2 Immunization policies

3.1.2.1. Policies in areas of high and intermediate endemicity

The consultation endorsed the WHO policy of including HBV immunization into the EPI for all infants in countries of high and intermediate endemicity (>2% prevalence of HBV carriers), but made the following further recommendations in order to achieve earlier control of adult, sexually transmitted HBV infection.

- (a) Infant immunization programmes will have little impact on sexual transmission for several decades. In areas where resources permit, and sexual transmission between adults is common, consideration may be given to the additional benefit of routine immunization in early adolescence until the first immunized infant cohort reaches adolescence.

- (b) Even in areas of intermediate or high endemicity, appreciable amounts of sexually transmitted HBV infection may occur in particular groups such as sex workers (both male and female) and homosexual and bisexual males. These groups may be frequent transmitters of infection to others. Under these circumstances targetted immunization programmes should be considered subject to accessibility and compliance of these groups.

3.1.2.2 Policies in areas of low endemicity

In areas of low endemicity, targetted immunization policies have been recommended by WHO and others but have rarely been implemented. There is little evidence that these have been effective in controlling sexually transmitted infection. The following recommendations are made:

- (a) In low endemicity areas, HBV is predominantly transmitted during adulthood. Therefore, when there is evidence that the disease burden is sufficient to warrant immunization of infants to prevent adult infection, an optimal strategy would be to implement routine adolescent immunization in conjunction with infant immunization until the first cohort of infants immunized reaches adolescence. Where routine immunization of infants is not yet feasible, routine immunization of young adolescents still is recommended.
- (b) Programmes should be strengthened to target high risk groups, important for sexual transmission, whose members can be identified and who are likely to be compliant. Under these circumstances it is particularly relevant to consider immunization schedules which may optimize compliance.

3.1.3. Optimum patient care

Realizing that resources for testing and counselling vary greatly throughout the world, the consultation also made recommendations for management of individual patients and their partners, under optimal circumstances.

- (a) National authorities should maintain an adequate system of disease surveillance, provide access to health care for actual or suspected cases of HBV infection and make provision for counselling HBV patients and their contacts.
- (b) Medical providers should be trained to assess their patients risk of infection with HBV and other STD, and those at high risk of HBV infection should be offered vaccination. Those at high risk include homosexual and bisexual males, sex workers and injecting drug users. Other high-risk groups may include heterosexuals with multiple partners, patients attending STD clinics, high risk adolescents, and certain travellers to endemic areas.
- (c) Sexual partners of acute HBV cases should be notified and immunization with HBV vaccine recommended. Although HBV-immune globulin is very expensive, some additional benefit may be obtained from its use in addition to vaccine. The appropriateness of determining the immune status of the contact will depend upon several factors including the need to avoid delay, the relative cost of testing and vaccination, the probability of prior infection, and the desirability of counselling partners on their infection status.

(d) Vaccine should be given to the susceptible sexual partners and members of households of chronic carriers. Such contacts have a high prevalence of HBV markers and therefore pre-vaccination screening for susceptibility may be cost-effective.

4. RECOMMENDATIONS FOR RESEARCH IN THE AREA OF HEPATITIS B AS A SEXUALLY TRANSMITTED DISEASE

4.1 Natural history and transmission

(a) Better define the chronic disease burden associated with adult infections through further studies on the natural history of HBV infection. Studies are needed to determine the proportion of chronic infections that result from both clinical and subclinical acute infections. Such studies should also include whether the outcome of infection is affected by the presence of low levels of anti-HBs resulting from postexposure immunoprophylaxis.

(b) Further studies are needed to elucidate the role of different sexual practices in the transmission of HBV between heterosexuals, and to determine the risk of infection per single heterosexual encounter as a function of duration of infection and relative infectivity.

(c) Focus on data resulting from ongoing (current) studies that measure duration of immunity after infant, childhood or adolescent immunization to determine if booster doses will be required to protect against infection when a person reaches sexually active age.

4.2 Epidemiology

(a) Determine the burden of disease associated with sexual transmission of HBV in relation to other modes of transmission in different populations so that priorities can be set for vaccination strategies.

(b) Determine the most cost-effective approach to establishing adequate surveillance systems in different populations that will detect changes in epidemiologic trends as a way of evaluating intervention strategies as implemented. Such systems might be based on population-based serologic surveys and/or on surveillance for acute cases of disease.

(c) Establish surveillance programmes to determine the amount of chronic liver disease due to HBV infection in different populations.

4.3 Operational issues

(a) Determine the level of knowledge of health care providers and the target populations concerning risk of sexual transmission and means of prevention.

(b) Design and implement demonstration "targetted immunization programmes" that will include evaluation of compliance, coverage and cost. Include in these programmes studies of alternate schedules that might influence compliance in different populations (adults versus children) and social marketing techniques that use incentives to sell "products" of high social value.

(c) Any vaccination programme should include the design and implementation of evaluation methodologies to assess the process and outcome of vaccination programmes. These should include use of surveillance and case-control methodologies to assess outcome.

4.4 Cost-effectiveness

Studies will be needed to determine the cost of acute and chronic infection as well as the cost of alternative vaccination strategies in different populations.

More complete evaluation of the cost-effectiveness of various post exposure immunoprophylaxis strategies is also needed.

LIST OF PARTICIPANTS

Temporary Advisers

Dr M. ALTER, Chief, Epidemiology Section, Hepatitis Branch, Centers for Disease Control, 1600 Clifton Road NE, Atlanta, Ga 30333, USA

Dr R. ANDERSON, Epidemiology, Imperial College of Science and Technology, South Kensington, Prince Consort Road, London SW7, UK

Dr L. GAYOTTO, Faculty of Medicine of the University of Sao Paulo, Avenida Dr. Arnaldo, 455, 01246 Sao Paulo, Brazil

Dr R. GILSON, Lecturer in Genito-Urinary Medicine, University College & Middlesex School of Medicine, James Pringle House, The Middlesex Hospital, London W1N 8AA, UK

Dr GOH Kee Tai, Head, Quarantine & Epidemiology Department, Ministry of the Environment, Environment Building 22-00, 40 Scotts Road, Singapore 0922, Singapore

Dr S. HADLER, Immunization Division, Center for Prevention Services, Centers for Disease Control, 1600 Clifton Road NE, Atlanta, GA 30333, USA (Rapporteur)

Dr K. HOLMES, Director, University of Washington Center for AIDS and STD, University of Washington, Seattle, USA (Chairman)

Dr F. MHALU, Department of Microbiology and Immunology, Muhimbili Medical Centre, Box 65001, Dar es Salaam, Tanzania *

Dr G. PAPAEOANGELOU, Professor, Department of Epidemiology and Medical Statistics, National Centre for Viral Hepatitis, Athens School of Hygiene, 52 Skoyfa St., Athens 11521, Greece

Dr P. PASQUINI, Istituto Superiore di Sanita, Laboratorio di Epidemiologia e Biostatistica, Viale Regina Elena, 299, 00161 Roma-Nomentano, Italy

Dr P. PIOT, Professor, Department of Microbiology, Institute of Tropical Medicine, Nationalestraat 155, 2000 Antwerpen, Belgium *

Dr A. TOUKAN, Professor of Medicine, Liver Unit, Department of Medicine, University of Jordan, P.O. Box 5192, Amman, Jordan

Dr A. TRAISUPA, Deputy Director General, Department of Communicable Disease Control, Davavesm Palace, Bangkok 10200, Thailand

Dr M. YANO, Director, WHO Collaborating Centre for Reference and Research on Viral Hepatitis, National Central Hospital, Kubarago 603-1 Omura City, 836 Nagasaki, Japan *

Dr I. WELLER, Academic Department of Genito-Urinary Medicine, University College & Middlesex School of Medicine, James Pringle House, The Middlesex Hospital, London W1N 8AA, UK *

* Unable to attend

WHO Secretariat

Dr A. Andjaparidze, Health Situation and Trend Assessment, Communicable Diseases, World Health Organization, Regional Office for South-East Asia, New Delhi, India

Dr Y. Ghendon, Microbiology and Immunology Support Services, Communicable Diseases, World Health Organization, 1211 Geneva 27, Switzerland

Dr F. Judson, Sexually Transmitted Diseases, Division of Communicable Diseases and Global Programme on AIDS, World Health Organization, 1211 Geneva 27, Switzerland (Co-Secretary)

Dr M. Kane, Microbiology and Immunology Support Services, Division of Communicable Diseases, World Health Organization, 1211 Geneva 27, Switzerland (Co-Secretary)

Dr B. Nkowane, Global Programme on AIDS, World Health Organization, 1211 Geneva 27, Switzerland

Dr P.-H. Lambert, Microbiology and Immunology Support Services, Division of Communicable Diseases, World Health Organization, 1211 Geneva 27, Switzerland

Dr A. Meheus, Sexually Transmitted Diseases, Division of Communicable Diseases, World Health Organization, 1211 Geneva 27, Switzerland

Dr R. Scott, Expanded Programme on Immunization, World Health Organization, 1211 Geneva 27, Switzerland

Dr G. Torrigiani, Division of Communicable Diseases, World Health Organization, 1211 Geneva 27, Switzerland

Dr M.H. Wahdan, Disease Prevention and Control, World Health Organization, Regional Office for the Eastern Mediterranean, Alexandria, Egypt