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## SEXUALLY TRANSMITTED DISEASES RESEARCH

Report of a WHO Working Group  
Geneva, 22-24 April 1991

### Programme for Sexually Transmitted Diseases

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## INTRODUCTION

The morbidity of Sexually Transmitted Diseases (STD) throughout the world is great and the needs of poor resource areas to develop STD control strategies are many. To develop appropriate and efficient strategies, however, additional knowledge is necessary. To advise the WHO/STD Programme on global STD research needs and their relative priorities a Sexually Transmitted Diseases Research Working Group comprised of an interdisciplinary group of scientists from both developing and industrialized countries and assisted by other WHO programmes, met April 22-24, 1991 in Geneva. Dr R. Henderson, Assistant Director-General of the World Health Organization, opened the meeting on behalf of the Director-General.

The group took direction, in part, from two sources. The first was a report of a meeting of a Consultative Group to the WHO STD Programme convened in September 1989 to systematically review STD research needs. (Document WHO/VDT/89.448) This meeting also consisted of an interdisciplinary group of scientists from both developing and industrialized countries and focused upon research needs in developing countries to achieve STD control. Four broad areas of research were highlighted (biomedical, clinical and epidemiological, behavioural and operations research) and used to consider the overriding themes of expansion of inter-regional and inter-disciplinary collaborations, strengthening of research institutions, development and strengthening of research training, facilitation of technology transfer and utilization of marketing systems.

The second source was a meeting of the Research Sub-committee of the AIDS/STD Task Force of WHO convened in July, 1990 to consult on Global Strategies for the Coordination of AIDS and STD Control Programmes (Working paper by S. Aral, M. Laga and J. Wasserheit, unpublished). This group, recognizing the significance of HIV as a sexually transmitted agent and its relationship to other STD, identified 69 HIV and/or STD research issues. The majority of the priorities were found to overlap because: 1) 70-80 percent of HIV infections are spread by sexual contact, and 2) STD and HIV infections mutually facilitate each others transmission.

## OBJECTIVES

The objectives of the Working Group were to review global STD research needs, and then to recommend research priorities for the WHO/STD Programme, which, in the context of developing countries emphasized cost/effective prevention, case detection and management, surveillance, and programme evaluation. Throughout the meeting the relevance of research to practical, operational issues was stressed. The Working Group considered research needs identified by the WHO Consultative Group's comprehensive review in 1989 (see above), and by members through their individual presentations

during this meeting. The unique global role that the WHO/STD Programme can play in encouraging and coordinating STD research and control efforts, as well as in providing guidance to donor agencies wishing to support STD research in developing countries, was acknowledged. The relationship between proposed research initiatives and priority areas identified by the Global Medium-term Programme for the Prevention and Control of STD 1990-95 was reviewed (Document WHO/VDT/88.1).

#### RESEARCH REVIEW AND SELECTION PROCESS

Recognizing the large numbers of potential projects, the Working Group used the following value factors to select priority research projects for the developing world:

- \* Impact on prevention and control of sexually transmitted infections (STI);
- \* Cost: vis-à-vis total cost, cost-effectiveness, and cost-benefit;
- \* Feasibility, taking into account such issues as cultural acceptability;
- \* Potential availability of a sponsor;
- \* Generalizability.

Basic research in areas such as pathogenicity, pathobiology, and vaccine development, although quite important, were not further considered because other institutions were seen as better suited for these studies.

#### RESEARCH SUBJECTS

Four broad and overlapping categories of research were identified: 1) operations research; 2) patient management; 3) behaviour; and 4) epidemiology. Within these categories, 20 priority research subjects were selected and posed as research questions. Many of the research questions in turn can be addressed in several ways, allowing flexibility for individual investigators and adaptation to local needs. Some research subjects include topics to guide researchers in directions the Working Group wished to emphasize. Examples are presented where the Working Group believed this might enhance understanding of the research intent. Except for 10 research subjects designated by an asterisk (\*) as having marginally

higher priority, no efforts were made to assign relative value.

The Working Group stressed that its priority research subjects are not the only ones which need to be studied. Both the report on Sexually Transmitted Diseases Research Needs and the working paper of the Research Sub-Committee of the AIDS/STD Task Force of WHO mentioned in the introduction, contain many others, some of which will appropriately be assigned a higher priority by other programmes.

## 1. OPERATIONS RESEARCH

- \* Surveillance: What are the most cost-effective, appropriate, timely, specific, and sensitive surveillance systems for STI and their sequelae as well as for related changes in sexual behaviour.

Rationale/Impact: Surveillance is often the tool by which interventions are chosen. Nonetheless, simple surveillance systems for developing countries which yield reliable and comparable data are not available. They are needed to assess long term morbidity trends, evaluate results of intervention programmes, and target resources.

- \* Rapid assessment of STI: This is a specialized and short term approach with more limited surveillance objectives. What methodologies can rapidly assess the overall current STI situation in a country, and thereby provide guidance for more targeted research, STI control priorities, and intervention efforts?

Rationale/Impact: Many countries have perceived or actual high rates of STI, but lack a sufficiently clear and detailed "picture" of STI epidemiology, sexual behaviour, and services to rationally target intervention strategies. How can a comprehensive review of these and other areas be rapidly and efficiently conducted? What approaches to STI control should be considered, how should they be assessed, and what tests should be offered to individuals in formulating a country specific STI control plan?

- \* Health care delivery systems: What are the most effective and efficient means of delivering care for STI. A variety of potential options should be considered ranging from use of community health workers in remote areas to partnerships with private physicians in cities. Also, nontraditional deliverers of care should not be ignored. Needing assessment is the effectiveness of categorical STI care compared with care integrated within primary health, family planning, and antenatal

clinics. Important characteristics to evaluate are:

- a. Cost and cost-effectiveness;
- b. Acceptability to persons at greatest risk of STI;
- c. Effectiveness in reducing rates of specific STI.

Rationale/Impact: Health care systems in developing countries are extremely diverse and delivery of primary care, including care for STI, will need to be individualized. Nevertheless, a broad common ground exists and the availability of several effective models for delivery of STI services could form the structural basis for country specific improvement of STI control programmes.

Involvement of informal sources of health care: What strategies could increase the contributions to STI control efforts of pharmacists, injection services, traditional healers and other informal sources of health care.

Rationale/Impact: The health care delivery systems of developing countries are extremely diverse and almost universally include informal sources of health care. Some of this care may be effective (e.g., appropriate antibiotics obtained from pharmacists or traders), while some is not. Regardless, every contact with these sources by individuals at risk of STI provides an opportunity for more effective care. The enhancement of informal sources of care may provide an inexpensive, yet effective means of increasing health care delivery for STI.

Prevention of ophthalmia neonatorum: What are the cost-effectiveness and cost-benefit of existing intervention strategies, and the barriers to effective implementation.

Rationale/Impact: Control strategies exist to prevent gonococcal and, to a lesser extent, chlamydial ophthalmia neonatorum using screening and treatment of pregnant women and/or eye prophylaxis in the newborn. Better documentation of effectiveness and costs of intervention strategies would enable rational revision and selection of protocols and encourage more widespread implementation by health care delivery systems.

- \* Control of syphilis in pregnancy: What are the cost effectiveness and cost-benefit of existing intervention strategies and the barriers to effective implementation?

Rationale/Impact: Control strategies exist to detect syphilis in pregnant women and prevent infection and serious disease in their unborn or newborn children. Better documentation of effectiveness and costs of intervention strategies would enable rational revision and selection of protocols and encourage more widespread implementation by

health care delivery systems.

## 2. PATIENT MANAGEMENT

- \* Algorithms for STD patient management: How can the field performance (e.g. diagnostic accuracy, costs, treatment efficacy, partner notification, and reinfection rates) of algorithms to diagnose and treat STI be evaluated and improved? The greatest need is for patient management algorithms for women and for individuals with genital ulcers.

Rationale/Impact: It is unlikely that in the near future sophisticated diagnostic tests will be available to much of the developing world's population. Hence, patient management will be guided by algorithms which are based upon risk factors, limited clinical findings, and limited laboratory support. It will be difficult to know how widely and confidently specific algorithms should be promoted and implemented until adequate field evaluations have been performed.

- \* Diagnostic tests: What are the performance characteristics and cost-effectiveness of various diagnostic tests when used in developing countries. Priority needs include simple, rapid, reliable and inexpensive tests for:
- N. gonorrhoeae, and Chlamydia trachomatis infections;
  - etiologic diagnosis of genital ulcers;
  - noninvasive diagnosis of STI in women;
  - sensitive, although not necessarily specific, screening or prescreening for inflammatory signs of STI e.g., leukocyte esterase.

Rationale/Impact: Many STI cannot be diagnosed in the developing world because of a lack of diagnostic tests and/or the ability to access the cervix. Consequently gonococcal and chlamydial infections, which are largely asymptomatic or nonspecifically symptomatic in women, remain untreated. Availability of simple, rapid, and inexpensive diagnostic tests would allow widespread population based screening as well as better case detection and more accurate diagnosis in individuals who seek health care.

- \* Treatment effectiveness: What are the best ways to monitor changes in antimicrobial resistance and in the effectiveness of regimens used to treat STI and syndromes? Areas for special emphasis:
- Surveillance of Neisseria gonorrhoeae and Haemophilus ducreyi resistance mechanisms, patterns and trends;
  - Evaluation of short-course or single-dose regimens;

- c. Evaluation of drugs and drug regimens potentially useful in developing countries;
- d. Treatment effectiveness in patients co-infected with HIV;
- e. Treatment safety and effectiveness in pregnancy.

Rationale/Impact: In many parts of the developing world the effectiveness of commonly used antimicrobial regimens is unknown. Even if effective initially, regimens may lose effectiveness rapidly because of intense antimicrobial pressure. Surveillance systems to assess the effectiveness of currently used or newly developed regimens are needed to permit control programmes to make timely adjustments in recommended treatments.

Partner notification: Which strategies of partner notification can best accomplish prevention, early case detection, and/or early treatment. Of particular interest are:

- a. Different cultural responses to partner notification and the possible adverse effects on women who notify their male partners;
- b. Measures of efficacy, including reduced reinfection rates and community STI burden.

Rationale/Impact: While partner notification is an important component of STI control programmes in some industrialized countries, it is not often practised in developing countries. Addition of culturally acceptable and cost-effective partner notification programmes could considerably reduce transmission of STI.

### 3. BEHAVIOUR

- \* Identification of and intervention in high risk groups: How can population groups at greatest risk of transmitting or acquiring STI be identified and what strategies will effectively and efficiently reach them to decrease infection rates? Examples of groups likely to transmit infections include prostitutes and truck drivers.

Rationale/Impact: In all countries some populations are at significantly greater risk of transmitting or acquiring STI than others (sometimes referred to as "core groups"). The identification and study of high risk groups would allow more effective targeting of STI interventions (including behavioural or educational) to groups responsible for disproportionate numbers of STI.

Identification of and interventions in groups at moderate risk: What strategies can identify and access groups at increased, but moderate risk of STI (e.g., spouses or customers of prostitutes or truck

drivers, individuals with multiple partners, tourists, migrants), and what are the most cost-effective interventions to decrease infection rates?

Rationale/Impact: Although members of "core groups" are at greatest risk of infection, there is a much larger and heterogeneous group at moderately increased risk of infection owing to living situations or sexual habits. Importantly, many of these individuals may not perceive themselves to be at increased risk. Research is needed to develop and evaluate strategies to identify these individuals, inform them of their risk, and institute behavioural change and cost-effective STI screening programmes.

- \* Health care seeking behaviours: What STI health care services are available; why and how do patients use them? Examples of health care services may include physicians, primary health care centers, pharmacies, drug traders and traditional healers. Of particular interest:
- a. What motivates persons to seek health care and how do they access it?
  - b. How do positive or negative experiences with the health care services influence subsequent health care seeking behaviours?
  - c. What are patient attitudes toward STI or the presence of suggestive symptoms?

Rationale/Impact: In most developing countries a variety of potential sources of health care exist ranging from self-treatment with herbs or medicines to technologically advanced hospitals, yet relatively little is known about the determinants of care-seeking behaviour, what obstacles patients face, or what negative experiences they have had. Better understanding of the knowledge, attitudes, beliefs and practices (KABP) which influence health care-seeking behaviours would help to design more effective health care services.

Other behaviour: Many aspects of sexual behaviour which contribute to transmission of STI have been incorporated into research priorities elsewhere in this report. While the Working Group wished to emphasize the fundamental importance of behavioural research, especially for non-HIV STI, it also wished to acknowledge the shared interests and responsibilities in this area of other WHO Programmes (e.g. Global Programme on AIDS; Special Programme of Research, Development, and Research Training in Human Reproduction; Maternal and Child Health; Adolescent Health) and chose not to include additional specific behavioural research subjects among its priorities.

#### 4. EPIDEMIOLOGY

- \* Female-controlled methods of primary prevention: What is the use-effectiveness of female-controlled methods of STI prophylaxis (e.g., female condoms and vaginal microbicides) in different cultures. What strategies can improve acceptability?

Rationale/Impact: Although condom campaigns have been widely implemented and variously successful, male condoms requires the man's willing participation. If effective female-controlled means of STI prophylaxis can be found they could greatly reduce the transmission of STI in the many situations in which male partners fail to assume responsibility for STI prevention.

Impact of HIV on other STI: What is the influence of HIV immunosuppression on the natural history of other STI including a more severe or prolonged course of disease (e.g., syphilis, genital HSV and HPV); higher treatment failure rates (e.g., chancroid, HSV infections); and accelerated course of disease (e.g., cervical dysplasia).

Rationale/Impact: There is increasing evidence that HIV infection adversely influences the course, treatment, and infectiousness of many other STI. Better understanding of these interrelationships at a clinical, biologic and epidemiologic level could lead to more effective interventions for both HIV and other STI.

Cofactors in transmission of STI: What are the interactions of other factors (e.g., the lack of circumcision, oral contraceptives, and cervical ectopy) in the transmission of STI?

Rationale/Impact: The transmission of STI may be enhanced by a variety of physical, hormonal and immunological factors, but the underlying mechanisms often are not understood or quantitated. Research is needed to answer questions which bear on the formulation of control strategies ranging from programmes to promote circumcision to alternative methods of birth control.

Impact of STI on pregnancy outcome: What is the impact of STI on fetal wastage, low birth weight, neonatal health, and maternal morbidity and mortality?

Rationale/Impact: The adverse effects of STI on pregnancy outcome have long been recognized but the extent of the problem in developing countries has been poorly determined. Better epidemiologic information would assist in targeting control measures to the STI producing the greatest morbidity.

Role of STI in ectopic pregnancy and infertility: What are the relative contributions of STI, childbirth, and abortion to subsequent ectopic pregnancy and infertility?

Rationale/Impact: Ectopic pregnancy and infertility are major problems in many parts of the developing world. Both are recognized complications of salpingitis which most often is caused by STI (principally N. gonorrhoeae and C. trachomatis), but also by other infections following childbirth or abortion. Effective interventions to prevent ectopic pregnancy and infertility requires a more complete understanding of etiology and epidemiology.

Epidemiology of HPV infection and cervical carcinoma: What is the magnitude of HPV infection and cervical carcinoma in the developing world, and what are cost-effective strategies to detect cervical dysplasia and carcinoma?

Rationale/Impact: The world's highest rates of cervical carcinoma are found in the developing world, but in many areas the epidemiology of cervical carcinoma and its relationship to HPV infection and other risk factors have not been well studied.

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