International Co-operative Study on Streptococcal Infections, Rheumatic Fever and Rheumatic Heart Disease in Asia

(Second Report)

Brief Report of a meeting held in Tokyo, Japan, March 8, 1981*

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THE international Cooperative Study on Streptococcal Infections, Rheumatic Fever and Rheumatic Heart Disease in Asia belongs among advanced programs of this kind that are being carried out in various parts of the world. This study, initiated and chiefly coordinated by Japanese specialists, has stemmed from the fact that the health and economic importance of rheumatic fever, rheumatic heart disease, acute glomerulonephritis and streptococcal infections was demonstrated to be high in a number of countries belonging to the WHO regions of South-East Asia and Western Pacific. Group A streptococci, which cause these diseases in man, are highly prevalent in these areas. The role of the group A streptococcus was greatly underestimated here in the past and the streptococcus problem therefore deserves special attention. Implementation of a research program conceived on an international scale has therefore been fully justified and continuation of activities along the lines of basic and applied research is also highly desirable in the future.

The geographic areas covered by the international cooperative study are of considerable concern to the WHO Headquarters, the respective WHO Regional Offices and the WHO Collabo-

rating Centre for Reference and Research on Streptococci. The international cooperative study is consistent with the WHO long-term program. The mutual links between the international cooperative study and other WHO activities have already been established and will further be corroborated.

This document represents a brief report on the proceedings of the meeting and the conclusions reached with regard to both the data presented and the proposals made for continuation of the study from 1981 onwards. It was agreed that detailed proceedings, in particular including in extensor the papers of the participants, would be prepared at a later date when all material had been collected. Furthermore, the possibility of preparing an article for publication in one of the Japanese journals was considered.

The General Aim, Special Objectives and Protocol of the International Cooperative Study, 1977-1980

The general aim of the international collaborative study was to establish the clinical, microbiological and epidemiological features of streptococcal infections in the particular area in order to advise on improved methods for diagnosis, therapy and prevention.

The objectives were to provide data on carriership rates for beta hemolytic streptococci in the throat and on the skin, on the incidence of streptococcal throat and skin disease, on the prevalence of serological groups of streptococci,

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*The meeting was convened by Dr. Y. Shiokawa, Chairman of the coordinating body of the international study. Among the eleven participants present were representatives from Japan and the Philippines. The representative from Indonesia could not attend but his data was made available. Dr. J. Rotta, the director of the WHO Collaborating Centre for Reference and Research on Streptococci, also participated in the meeting. The list of participants (in alphabetical order) was as follows: Dr. S. Hatano, Dr. N. Kosakai, Dr. S. Kawakita, Dr. S. Kodama, Dr. Y. Miyamoto, Dr. M. Okuni, Dr. T. Oda, Dr. J. Rotta, Dr. Y. Shiokawa, Dr. T. Takeuchi, Dr. J. Yason.

on the role of different environmental factors and on the ways of improving the management and control of streptococcal infections in the local conditions.

The *microbiological methods* and *epidemiological approaches* employed in the study were described in detail in the first document on the study prepared in 1977¹. These methods were based on conventional techniques used in most streptococcus laboratories and recently recommended in the WHO Manual of Microbiological Diagnostic Methods for Streptococcal Infections and Their Sequelae (WHO/BAC/80.1). There were, however, some differences in the microbiological methodology due to local conditions in the participants laboratories or to nonavailability of reagents for running specialized procedures of streptococcus bacteriology and serology. This variance has had no influence on the reliability and comparability of results.

In brief, in the *microbiological* part of the study specimens were cultivated on blood agar media, beta hemolytic streptococci were identified and were classified into groups by a serological method (direct slide agglutination technique employing a suspension digested by trypsin). The hemolysis inhibition test in Kobayashi's modification and the bacitracin test were employed in some instances for rapid screening for group A streptococci. The typing of group A streptococci was carried out by using the T typing system only. Factor anti-T protein sera were used.

For the determination of antibodies to streptococcal antigens, the most commonly used serological test in retrospective or indirect diagnosis of streptococcal disease was the antistreptolysin O assay. Other tests used by some participants were determination of anti-deoxyribonuclease B, anti-streptokinase and the streptozyme test.

The *epidemiological* components of the studies was consistent with the conventional requirements for adequate selection of population samples, decision on the time for sampling for the microbiological examination and the clinical follow-up. The results of all clinical, epidemiological and microbiological findings were recorded on specially designed forms. These forms were the Initial Recording Form, the Follow-up Recording Form and the Bacteriological and Serological Recording Form.

The studies were carried out in the following countries: Japan, the Philippines and Indonesia.

Summary of the Study

1) Prevalence of group A streptococcus carriership in school children, was approximately 10 to 40% and was essentially similar among the participating countries. Prevalence varied by season. It was high during the rainy months in Indonesia and the Philippines. It was high in winter in Japan. Higher prevalence was observed in the lower socioeconomic group in Indonesia and the Philippines (especially in the rainy season). Taking all these features of carriership into consideration, the most consistent predisposing factors for streptococcus carriership seemed to be crowded living conditions.

2) The majority of isolated streptococci belonged to group A. The second most frequent one was group G in these areas. There was a variation in predominant T types in the respective countries and in different seasons.

3) Prevalence of streptococci in the normal skin was low, i.e. under 2% in Jakarta. Infected skin was comparatively prevalent in the low socioeconomic group in the Philippines. In Japan, strains of streptococci isolated from normal skin were identical in T types to those from throat cultures. Contamination by the hands might be responsible for colonization of streptococci in the throat.

4) Previous studies in the selected groups of school children reported prevalence rates of rheumatic fever and rheumatic heart disease as 0.8 to 0.1 per thousand in Indonesia and the Philippines, and much less than 0.1 in Japan.

5) The low prevalence of rheumatic fever and rheumatic heart disease in Japan, compared with the higher prevalence rates in Indonesia and the Philippines in spite of the same carriership rates, raised questions on the possible contributing factors (e.g. host response and virulence of bacteria) to the occurrence of rheumatic diseases.

6) It was emphasized that the study had greatly contributed to knowledge on various facets of the streptococcus problem in Asia. The study had proved that a properly coordinated program provides valuable information on the magnitude of the problem and makes it possible to propose adequate clinical, microbiological and epidemiological methods of approach aiming at reliable diagnosis and more efficient control. Furthermore, competent decisions can be taken in health administration and reasonable planning can be undertaken on a national scale.

Activities Proposed for Continuation of the

International Cooperative Study in the Future

The research work accomplished during the four-year pilot projects carried out in the three participating countries, Japan, the Philippines and Indonesia, contributed considerably to knowledge on the complex streptococcus problem in that part of the world. The study proved that a joint collaborative program was feasible and was of great benefit for all participating countries. The ways for a useful and fruitful cooperation were established. Improved or new methods in streptococcus microbiology were introduced and optimal approaches to clinical and epidemiological investigations were identified. Close cooperation between clinicians, epidemiologists and microbiologists was carried into effect. Although the data and the experience derived from the pilot studies can already as they stand be used for considerable improvement of the health services at the primary health-care level and for implementing more effective diagnostic and preventive procedures, there are still a number of components of the complex streptococcus problem which require further basic and applied research before measures for fully satisfactory control of streptococcal infections, rheumatic fever and rheumatic heart disease can be formulated.

The proposals for the continuation of the international cooperative study are based on the information and experience provided in the previous four years study. The proposed points can be stated as follows:

1) Clinical, epidemiological and microbiological follow-up for *carriership* in school children should be continued in all places where the information on the role of particular factors is still incomplete, e.g. the role of season of the year, rural and urban living conditions, etc.

2) Assessment of the incidence of streptococcal *pharyngitis* and *impetigo* in children aged 6–15 years should be carried on for a period of 1 to 3 years. A selected sample of 200–400 individuals should be surveyed and children complaining of sore throat or skin infection should be examined clinically and bacteriologically. The strains isolated should be grouped and if possible typed.

3) A stepwise program for a mass screening for *rheumatic heart disease* in individuals aged 15–25 years should be developed. Obvious and suspected RHD cases should be conclusively examined in hospitals, all identified RHD cases should be registered and a long-term prophylaxis

program by penicillin for prevention of recurrent attacks should be launched. The practicability of a modification of the conventional program could be investigated (e.g. to carry out the prophylaxis only during the months of higher circulation of streptococci).

4) The natural history of *rheumatic fever* should be studied with regard to streptococcal infections. Fresh cases of RF (some 20 to 30 cases) should be subjected to long-term follow-up in order to identify the whole pathogenetic process of the disease from various points of view. Such information on the clinical and microbiological patterns of the disease is not available from tropical and subtropical areas and the data from Japan, Europe and the United States are incomplete. This study would require the use of refined clinical and laboratory procedures.

5) A program should be initiated for *disseminating the experience and knowledge* on improved methods of diagnosis, therapy and prevention derived from pilot studies to other parts of the respective countries. This could best be done by launching educational programs. To gain the support of policymakers would be essential for successfully coping with task. The cooperation would have to involve various specialists, e.g. cardiologists, pediatricians, school doctors, microbiologists and others.

6) Organization of *training course(s)* on microbiological and epidemiological topics of the streptococcus problem in countries participating in the international project would be very profitable.

7) The introduction of *refined or new laboratory techniques* including selected *simple tests* would deserve all possible consideration. This is in particular concerns the joint program of preparing M and SOF typing sera for the classification of selected, most important (rheumatogenic) types. The information on the prevalence of these types and on the changing prevalence patterns would be required when the alternative approach to prevention of streptococcus diseases by means of a polyvalent streptococcus vaccine for use in high-risk population groups had become feasible.

8) It would be desirable to pay more attention to *quality control* of the biological reagents used in streptococcus bacteriology and serology, no matter whether they are produced by commercial firms or advanced laboratories.

9) *Collaboration* of the countries partici-

pating in the international study with *WHO institutions* should be further stimulated and encouraged. It would be ideal to have one (possibly two) laboratory (ies) in each country carry out the functions of a reference streptococcus laboratory. These places should have properly established links to the WHO Collaborating Centre for Reference and Research on Streptococci.

10) Invitation of *other countries in Asia* e.g. Thailand, to join the international study under co-ordination from Japan should be considered.

11) Strengthening of *communication* between the participants of the study is essential.

Interim evaluations of the progress made in the studies and periodical data analysis, exchanged optimally at 2-year intervals, as well as the formulation of future program through workshop consultations of the participants are of the utmost importance.

REFERENCE

1. SHIOKAWA Y: On the international co-operative study on streptococcal infections, rheumatic fever and rheumatic heart disease in asia. *Jpn Circ J* **43**: 431, 1979

Detailed report will be available on request to the author.