DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Centers for Disease Control

# Memorandum

Date January 22, 1981

From Michael J. Rosenberg, Medical Epidemiologist
Family Planning Evaluation Division (FPED), CHPE

Subject Foreign Trip Report (AID/RSSA): London, England, December 8-9, 1980; Dacca, Bangladesh, December 12-19, 1980.

To William H. Foege, M.D.
Director, Center for Disease Control
Through: Horace G. Ogden, Director
Center for Health Promotion and Education (CHPE)

SUMMARY


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SUMMARY


I traveled to Bangladesh to continue CDC's technical assistance to the Government of Bangladesh in improving the country's sterilization program. At the Bangladesh Fertility Research Programme's Annual Conference, I presented a summary of the morbidity, mortality, and risk factors reflected in the Prospective Study of Sterilization performed earlier this year. With others involved in the study, the data underwent final review prior to preparation of a manuscript for publication. I also assisted the government and other donor agencies in formulating plans for changes in the program which are being initiated largely on the basis of CDC's recent intensive efforts at identifying problems with the program and steps which might be taken to improve its safety. Plans are now being finalized for a large-scale training program, involving both physicians new to the program and those already practicing sterilization, in aspects of patient selection and followup, technical performance, emergency procedures, and use of drugs. The new program will be summarized in a manual which is now being developed. We also made initial plans for a national sterilization conference to bring together all the physicians in Bangladesh who perform sterilizations to review recent research and to introduce and review proposed changes in the program. As a result of this attention, Bangladesh has one of the most intensively studied sterilization programs of any country and should be able to establish a standard of sterilization safety for developing countries.

I also stopped in London to bring Dorine Kramer, on assignment to International Planned Parenthood Federation from CDC, up to date on the sterilization program in Bangladesh.

## I. PLACES, DATES, AND PURPOSE OF TRAVEL

London, England, December 8-9, 1980: to consult with Dorine Kramer, M.D., of International Planned Parenthood Federation, regarding results of the Prospective Study of Sterilization in Bangladesh and status of plans for implementing changes in the country's sterilization program.

Dacca, Bangladesh, December 12-19, 1980: to present the results of the Prospective Study of Sterilization at the Fifth Annual Contributors' Conference of the Bangladesh Fertility Research Programme and to assist with implementation of changes in the national sterilization program.

## II. PRINCIPAL CONTACTS

Bangladesh Ford Foundation

Tony Measham, M.D., Representative for Population, Health, and Nutrition
Jalaluddin Akbar, Research Assistant
Nicholas Cohen, M.B.B.S., Medical Consultant

Bangladesh Fertility Research Programme (BFRP)

Shafiqur Rahman, M.B.B.S., Medical Consultant

U.S. Agency for International Development (USAID), Dacca

Charles Gurney, Chief, Population, Health, and Women's Division
Carol Carpenter-Yaman, Ph.D., Population Officer
John Fishburne, M.D., Consultant

Government of Bangladesh

Col. Hashmat Ali, Director of Training, National Institute of Research and Training
Narghis Akhtar, M.B.B.S., Director of Service and Training
Brigadier Shalira Huq, Chief Physician, Bangladesh Armed Forces

International Project, Association for Voluntary Sterilization (IPAVS)

Terry Jezowski, Representative for Asia
Russ Vogel, Assistant Representative for Asia

International Center for Diarrheal Disease Research (ICDDR)

Jim Phillips, Ph.D., Demographer
Roger Glass, M.D., Scientist
Susan Zanicki, M.S., Research Associate

International Planned Parenthood Federation (IPPF)

Dorine Kramer, M.D., Medical Epidemiologist

III. ACCOMPLISHMENTS

A. Prospective Study of Sterilization

The CDC has assisted with a prospective study to define the types and rates of complications associated with vasectomy and tubectomy in Bangladesh . Information was collected over a 5-month period from 41 sterilization centers throughout Bangladesh. Details of the study's design, field work, and results are contained in earlier trip reports (see Rosenberg MJ, trip reports of April 22, July 30, and October 30, 1980). It is the first prospective study of sterilization to be performed in a developing country.

Three papers based on data from the Prospective Study of Sterilization (PSS) were presented at the Bangladesh Fertility Research Programme's Annual Conference: I reviewed the morbidity, mortality, and risk factors associated with sterilization; Anthony Measham reviewed the demographic impact of the program, and Hasina Banu discussed characteristics of patients undergoing sterilization. All generated moderate interest in individual discussions following the presentations.

While in Dacca, I also reviewed data from the PSS with Jalal Akbar and Hasina Banu to make final corrections prior to tabulation for publication. For the first time, we also determined the interview followup rate to be 93 percent of patients selected to be interviewed. I think this reflects a superb effort on the part of the field team and is an outstanding rate considering the inherent difficulty of field work in Bangladesh. Upon further review of the data, I was also pleased with its excellent consistency and quality. A plan for written dissemination was worked out between researchers involved in the project which calls for three basic pieces: service characteristics of patients and facilities, factors affecting patient acceptance, and significance of sterilization program to Bangladesh will be written by Drs. Kuhn and Jabeen, demographic impact of program by Dr. Measham, and risk factors and complication rates by me. In addition, we agreed that there is sufficient data material for additional papers, and each of the participants was encouraged to stake out an area based on his/her interests.

B. Sterilization in Bangladesh

I attended a meeting of the government's Technical Committee, the Branch of the Ministry of Population which decides matters such as how sterilizations are performed and which drugs are used in government centers. At the meeting, the recommendations of John Fishburne, M.D., regarding changes in the use of medication and techniques were discussed and adopted. These recommendations were based largely on the strength of the PSS data and of CDC's and Dr. Fishburne's work which demonstrated overuse of sedatives as the major contributor to sterilization deaths in the country. I also presented a summary of the findings of the PSS regarding types, doses, and routes of sedative medicines which were used as well as details of the four deaths in the study due to respiratory arrest because of oversedation.

The Committee also discussed the use of prophylactic antimicrobials and the possibility of using a new agent, trimethoprim-sulfamethoxasole (TMP-SMX) in place of penicillin or tetracycline, which are currently used. I summarized the results of the PSS, which indicate that 70 percent of patients received tetracycline and the remainder penicillin, and that the complication rates did not vary according to which drug was used or if women reported taking the drug after leaving the sterilization center or not. I interpret this as indicating that the most important time for receiving the prophylaxis was immediately following the procedure, since most women received their first dose before leaving the center, and that use of antimicrobial prophylaxis seems to be more dependent on use during the peri-operative period than in the week following the operation. I recommended to the Committee that prophylactic antimicrobials be continued because of the frequently adverse conditions under which sterilizations are performed. Following my return to the United States, I was able to investigate the possible use of TMP-SMX more fully and make similar, more definitive recommendations (Appendix A).

The meeting also formalized the commitment of the Bangladeshi Government to move forward with plans at establishing training programs for new physicians as well as those already practicing sterilization. Plans were made for establishing 12 training centers throughout the country. Initially, trainers from those 12 centers will be brought to Dacca to work with physicians from the Bangladesh Association for Voluntary Sterilization, and those physicians will then establish ongoing training programs for their respective areas. A commitment was also made to sponsoring a national sterilization conference for all physicians who practice sterilization in the country at which recent research can be reviewed and changes in the program can be introduced and reviewed.

A second organizational meeting to discuss and refine plans for training and the conference was held between representatives of BAVS, the Ford Foundation, IPAVS, USAID/Dacca, and CDC. High level

support has been assured by the Secretary of Health and Minister of Population of Bangladesh with funding assured by FPIA and IPAVS. We agreed that BAVS should be the primary agency providing technical support to the Government of Bangladesh in organizing the meeting, and Dr. Azizur Rahman agreed to be Chairman. The chief purpose of the Conference is to allow the opportunity for the physicians who perform sterilizations to become aware of the problems which have been identified through recent research and to introduce new government policy designed to address those problems. The Conference will also provide a forum for physicians from the field to discuss problems, develop a feeling of participation in improving the country's program, and will instill a sense of pride in the country's efforts at improving the program.

I developed a preliminary outline of the scientific schedule for the 2-day Conference, which calls for the first day to review research and discuss the problems identified and introduce consequent changes. The second day will be spent reviewing the changes in detail and going over the comprehensive sterilization manual which is now being formulated based on BAVS practices. Small group sessions will be part of the activities in order to provide an opportunity to gauge the impact of the material and to allow interchange of ideas among physicians. It was tentatively agreed that CDC should participate in the Conference by presenting the results of the PSS and the investigation of sterilization-related deaths as well as leading some of the small group sessions.

C. Investigation into Sterilization Deaths

Based on field investigation into sterilization deaths (Grimes DA, Peterson H: CDC RSSA trip report of September 18, 1980), a manuscript was written for publication. I reviewed the draft with Dr. Kahn and Dr. Measham and together we made final corrrections and received Bangladeshi approval for its publication. The article has since been submitted to Lancet.

D. Future Population Research in Bangladesh

I discussed with Anthony Measham and Jim Phillips the possibility of performing a followup study on women who have been sterilized in Bangladesh to determine the failure rate. ICDDRB has complete followup records on approximately 2,000 women who have been sterilized over the past 2 years in Matlab thana. Cheng et al (Sterilization failure in Singapore, Studies in Family Planning 8:109, 1977) estimate the failure rate for tubal ligation at 0.5 percent, meaning that less than one pregnancy would be expected from this group, making it too small to yield reliable numbers. Tony and I discussed the possibility of followup elsewhere in the country, but the limiting factor seems to be the paucity of data on residence which is kept by most government centers. Better records are generally kept by BAVS, but we were not able to determine how difficult it might be to locate women 2 or more years after such a

procedure. We decided that the best way of testing the feasibility of such a study would be to go the field to examine the records and attempt to locate some of the women. Jalal Akbar has agreed to make such an attempt over the next few months, allowing us to gauge the degree of difficulty of such a study and to make estimates about how many women we need to attempt to locate, how long it will take, and how much it will cost.

E. Discussions at International Planned Parenthood Federation

I stopped on the way to Bangladesh to bring Dorine Kramer of IPPF up to date on sterilization events in Bangladesh. I briefed her on the proposed sterilization conference and my proposals for changes in the program. She indicated that IPPF will probably be interested in sending an observer to the sterilization conference as part of their efforts at identifying sterilization deaths throughout the world.

Michael Rosenberg

Michael J. Rosenberg, M.D., M.P.H.

APPENDIX A

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Centers for Disease Control
Atlanta, Georgia 30333

January 9, 1981

Col. Hashmat Ali
Director General
NIPORT
Azimpur
DACCA

Dear Colonel Ali:

Following the discussions of the Technical Committee regarding the use of prophylactic antibiotics, I have looked into the possibility of using trimpethoprimsulfamethoxazole (TMP-SMX) for sterilizations in Bangladesh. As you know, TMP-SMX is a fixed combination of 80 mg. of trimethoprim and 400 mg. of sulfamethoxazole which is marketed in the United States under the names Septra and Bactrim.

The prospective study of sterilization in which I was involved demonstrated that urinary tract infection is probably the most common infectious problem associated with sterilization in women. The reason I say probably is that we were not able to document infection, and symptoms are a notoriously poor indicator of infection. Let us assume for the moment, however, that we wish to address this potential problem. The drugs recommended for treatment of acute, uncomplicated urinary tract infection (UTI) are sulfisoxazole, ampicillin, or amoxicillin (Med. Letter 22:5, 1980). As the enclosed antibiotic sensitivities (from Hoeprich, Infectious Diseases) indicate, these drugs will cover about 80% of such infections, and I think these sensitivities are similar to those I would expect in women undergoing sterilization. The advantage of adding trimethoprim to sulfisoxazole is that the synergistic combination will cover organisms which are uncommon in acute UTIs but which are sometimes found in chronic and recurrent UTIs. In fact, TMP-SMX is not approved for use in acute, non-complicated UTI in the United States, and a recent review states, "Because alternative regimens employing less expensive drugs (i.e., sulfisoxazole) are as effective as TMP-SMX, and because it seems reasonable to restrict the use of TMP-SMX to clinical situations for which it is uniquely qualified, there seems to be little reason to employ conventional doses of TMP-SMX for such infection" (New England Journal of Medicine 303:426, 1980).

We should also consider whether there are any disadvantages to using TMP-SMX for routine prophylaxis. TMP-SMX will not cover Staphylococcus or Clostridium, the two organisms of primary concern in Bangladesh (see my trip report, page 11). In fact, the only licensed use of TMP-SMX in the United States other than chronic UTI is for the extremely rare pneumonia due to Pneumocystis carinii which is not relevant to sterilization patients. Another consideration is that TMP-SMX reaches easily detectable concentrations in breast milk, amniotic fluid, and in fetal serum (Ann Int Med 91:420, 1979), and is believed to be teratogenic (Septra package insert). Finally, I checked with a local pharmacy to determine the cost of three different treatments using three therapies:

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|---|---|
| TMP-SMX, 1 tablet twice a day for 10 days | $7.00 |
| ampicillin, 250 mg. four times a day for 10 days | $4.68 |
| sulfasoxazole, 500 mg. four times a day, 10 days | $5.00 |

These prices would undoubtedly be different in Bangladesh, but I suspect TMP-SMX will remain considerably more expensive. TMP-SMX may be also more difficult to obtain locally, while I believe both tetracycline and ampicillin are manufactured in Bangladesh.

Another consideration is whether there is reason to believe the current regimen of tetracycline or ampicillin is ineffective. As I reviewed for the Technical Committee, the prospective study of sterilization revealed no difference in the incidence of urinary tract complaints among the women who received antibiotics but admitted not taking them after leaving the sterilization center as compared with the women who did take the antibiotics. Nearly all women who complained of urinary problems had them resolved by the time our interviewers reached them two weeks after the operation. Thus, this information suggests to me that there is no clear indication that the current regimen is inadequate, although we both know these indications are not as clearcut as we would like them to be.

Thus, I feel that either ampicillin or tetracycline should continue to be used for prophylaxis because of their broad spectrum and low cost. Between the two, I would tend to favor ampicillin slightly because of tetracycline's danger of permanently staining teeth if taken by children. Ampicillin is also recommended as a prophylactic for abdominal surgery by the Veterans Administration Committee on Antimicrobial Drug Usage (JAMA 237: Supple, 1977). Although this recommendation assumes bowel surgery, sterilization involves many of the same organisms. Ampicillin use thus also guards against surgical accidents involving the bowel. As timing goes, the Medical Letter (21:73, 1979) recommends that the antimicrobials be given 1 to 2 hours before the operation, which is enough time to achieve therapeutic drug levels in the wound during the procedure, but not enough time to select bacteria resistant to the drugs. They also recommend that prophylactic drugs be stopped within 24 hours of the procedure, since continuing prophylaxis increases the risk of drug toxicity and bacterial superinfection but does not reduce the incidence of subsequent infection (Ann Surg 189:691, 1979). If such a regimen were to be established, the cost of antimicrobials would drop sharply.

I hope this information will be useful to you and the Technical Committee. If I can help further, please let me know.

Sincerely yours,

Michael J. Rosenberg, M.D.
Medical Epidemiologist
Program Evaluation Branch
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cc:
Anthony Measham, M.D.
Carol Carpenter-Yaman, Ph.D.
Roger W. Rochat, M.D.
Susan E. Holck, M.D.