

PD - AAM - 063

ISN 15018

9320502

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
CENTER FOR DISEASE CONTROL

TO : William H. Foegen, M.D.
Director, Center for Disease Control (CDC)
Through: Philip S. Brachman, M.D.
Director, Bureau of Epidemiology

DATE: July 3, 1980

FROM : Michael Rosenberg, M.D., M.P.H.
Family Planning Evaluation Division

SUBJECT: Resources Support Services Report (RSSR/AID): London, England, April 29
and May 15, 1980; Dacca, Bangladesh, May 2 - 13, 1980; Boston, Massachusetts,
May 16, 1980.

	<u>Page</u>
SUMMARY	
I DATES AND PLACES	2
II PURPOSES	2
III CHIEF CONTACTS	3
IV ACCOMPLISHMENTS	4
A. Prospective Study of Sterilization	4
1. Background of Request	4
2. Progress to Date	4
3. Survey of Emergency Equipment	5
4. Financial Status	5
5. Future CDC Involvement	6
B. Investigation of Alleged Sterilization Deaths	6
1. Background of Request for Assistance	6
2. Sterilization Background	6
3. Results	8
4. Discussion	9
5. Conclusions and Questions Raised	10
C. Seminar on Choosing the Number of Subjects for a Study	13
D. Work on Manuscripts Concerning Abortion in Bangladesh	14
E. Discussion with International Planned Parenthood Federation	14
F. Discussions with Peter Layde, M.D.	14
G. Discussions with Ken Rothman, Dr.P.H., and Olli Miettinen, M.D.	14

SUMMARY

This trip was chiefly to monitor the progress of the Prospective Study of Sterilization (PSS) being conducted with CDC assistance under a grant to the Bangladesh Fertility Research Programme. It is the first attempt to obtain national sterilization morbidity data in Bangladesh. Information on each patient's background and operative course have now been collected by 41 sterilization centers on 2,569 tubal ligation and 205 vasectomy patients, and a sample of 1,550 (60.3%) and 104 (50.7%), respectively, of these patients have been located by field workers two weeks after

discharge to identify problems which may have since developed. These centers have detected three tubal ligation and no vasectomy deaths, yielding a tubal ligation death-to-case rate of 11.7 (95% confidence interval, 4.0 to 34.3) per 10,000 procedures. All three deaths were apparently due to respiratory arrest at the time of operation. Among preliminary hand tabulations of a sample of 333 follow-up vasectomy and tubal ligation questionnaires, the most common postoperative problems were weakness (47%) and dizziness (44%). These were also the most common problems in the control period before the operation (15% and 11%, respectively). Indications of urinary tract infection occurred in less than 1%, and of wound infection in 2%. Telephone conversation on May 27th following further field work revealed one additional death (about which details are unknown) in 3,494 procedures, a sterilization death rate of 11.5 (95% confidence interval, 4.5 to 29.4) per 10,000 procedures.

The study also includes a survey of emergency equipment in sterilization centers. What I consider the most important single item for resuscitation, either an Ambu bag or emergency airway, was present in only 35% of the 37 of 41 study centers which responded.

I was also asked to conduct preliminary epidemiologic investigation into deaths occurring among sterilization patients in Bangladesh. During January-December 1979, the Government of Bangladesh received reports from district health officers of 13 deaths associated with tubal ligation and 5 deaths associated with vasectomy. These government figures indicate that the tubal ligation death-to-case rate is 1.2 per 10,000 procedures and for vasectomy 2.0 per 10,000 procedures. These deaths represent underreporting of an unknown magnitude. A tabulation of all alleged sterilization deaths beginning in November 1978 has been compiled along with frequently conflicting reports of each from a variety of sources which will be reviewed with clinicians in the United States. Based on my investigation and experience with sterilization and medical practice in Bangladesh, preliminary suggestions are made for improving the program. Epidemiologic assistance by the CDC should be continued to assure development of optimal performance standards and methods for their implementation.

While in Bangladesh, I also worked with others on the development of manuscripts concerning abortion in Bangladesh and presented a seminar on selection of study sample size at the International Center for Diarrheal Disease Research. I also met with others enroute to and from Bangladesh regarding other manuscripts in progress and briefed the medical director of International Planned Parenthood Federation on my work in Bangladesh.

I. DATES AND PLACES

London, England - April 29, May 5, 1980
Dacca, Bangladesh - May 2 - 13, 1980
Boston, Massachusetts - May 16, 1980

II. PURPOSES

London: To consult with Peter Layde, M.D., of the CDC, regarding manuscripts in progress, and with Pramilla Senanayake, M.D., Medical Director of International Planned Parenthood Federation, regarding my work in Bangladesh.

Dacca: To consult with the project staff of the Prospective Study of Sterilization regarding progress of the study, and with John Dumm and Charles Gurney of U.S. Agency for International Development, Dacca, regarding the sterilization program in Bangladesh and AID's efforts to help improve the program.

Boston: To consult with Ken Rothman, Dr.P.H., and Olli Miettinen, M.D., of the Harvard School of Public Health, regarding a paper on epidemiologic methodology in progress.

III CHIEF CONTACTS

Bangladesh Fertility Research Programme (BFRP)

Atiqur Rahman Khan, M.B.B.S, Director
Hasina Banu, M.A., Sterilization Project Director
Farida Akhtar Jahan, Data Coordinator
Pryabash Sarkar, Field Supervisor
Yousuf Choudhury, M.S., Data Analyst

Ford Foundation

William Fuller, M.B.A., Representative
Jalauddin Akbar, Project Consultant
Tony Measham, M.D., Representative

International Center for Diarrheal Disease Research, Bangladesh (ICDDR,B)

Roger Glass, M.D., Scientist
Barbara Stoll, M.D., Scientist
Susan Zamicki, M.P.H., Research Associate
Majid Molla, M.B.B.S., Scientist
K.M.S. Aziz, M.B.B.S, Scientific Director
Bucky Greenough, M.D., Director
Lincoln Chen, M.D., Scientific Director
Jim Phillips, Ph.D., Demographer

Sir Salimullah Medical College

Suriya Jabeen, M.B.B.S., Professor of Obstetrics and Gynecology
M. Abdullah, M.B.B.S., Registrar in Obstetrics and Gynecology

United Nations Family Planning Agency

Coke McCord, M.D., Medical Advisor

United States Agency for International Development, Dacca

John Dumm, Population Officer, Division for Population, Health, and Women's Affairs
Charles Gurney, Chief, Division for Population, Health, and Women's Affairs

Harvard School of Public Health

Ken Rothman, Dr.P.H, Associate Professor of Epidemiology
Olli Miettinen, M.D., Professor of Epidemiology

IV. ACCOMPLISHMENTS

A. Prospective Study of Sterilization

1. Background

This nationwide surveillance for complications of sterilization procedures was funded by the Program for the Initiation and Adaptation of Contraceptive Technology in a \$26,087 grant to the Bangladesh Fertility Research Programme. It was initiated in order to define the rates and types of complications which result from sterilizing operations in Bangladesh in response to concern over the possibility of preventable complications. Six field teams collect information from 41 sterilization centers which were selected to include a mixture of centers doing a high and low volume of sterilization. It is being conducted with CDC assistance and is the first prospective national sterilization surveillance to be performed in Bangladesh. Data collection is accomplished in two phases. First, information on the patient's pre-, intra-, and postoperative condition until the time of discharge is recorded. Two weeks after surgery, field workers locate and interview a sample of patients to determine whether any further complications have developed. The study's design is detailed in an earlier report¹.

2. Progress to date

Two months of data collection have been completed as of April 15th. After the first two 14-day trips for field work (February 15-29, March 1-14), it became apparent that unanticipated travel delays required more than 2 weeks to complete followup. The duration for each circuit of sterilization centers on each of the six teams' routes was increased to 28 days, and the third round of data collection was performed between March 15 and April 14th. Following that round, we had collected information on 2,569 tubectomies and 205 vasectomies, and of these, follow-up questionnaires were administered to 1550 (60.3%) tubectomy and 104 (50.7%) vasectomy patients (Appendix A).

Data collection has been hampered by two strikes. The first was of clerical workers in the sterilization centers during the first 2 weeks of April. This did not severely handicap collection, however, as initial information was recorded mainly by non-clerical personnel. The field team also relies mostly on other persons to help locate sterilization clients for followup. The second strike began the last week in April and by the middle of May had slowed the number of sterilizations to a trickle.

¹Rosenberg, MJ, Gould P: Memorandum to William F. Foegel, April 22, 1980

Without the help of the striking workers, it also became nearly impossible for our field workers to locate patients operated on before the strike for followup. At this time, it is difficult to judge the likelihood of strike resolution in the near future. Those field teams idled by the strike have been recalled to Dacca to assist with coding until the strike is resolved. If the strike is resolved and sterilization performance reaches prestrike levels by late May, sufficient time and funds remain to send the team to the field for one additional 28-day round of data collection. Field work will become severely impaired by the monsoon season which generally begins in mid- to late June so that collection of follow-up questionnaires will have to be terminated by then. However, the initial information which is recorded by the sterilization center personnel, will continue for several additional weeks if sufficient funds remain.

On this trip, the coding manual underwent additional changes to improve clarity and complete coding categories which were possible only after review of the initial data. Coding was initiated after these changes. At the time of my departure, 2,322 forms had been edited; of those 85% have been coded, and 9% have been punched into a diskette for eventual transfer to tape.

3. Survey of Emergency Equipment

We also surveyed emergency equipment available at the time data collection was begun (mid-February 1980). I feel that the two most important pieces of emergency equipment are an emergency airway or Ambu bag for resuscitation and a narcotic antagonist to neutralize the respiratory depressive effects of pethidine (meperidine); these were present in only 35% and 43% of centers, respectively. The tabulation of equipment is included as Appendix B and reflects a general shortage of emergency equipment. We expect that this study will help determine priorities for providing additional emergency equipment by documenting causes of death.

4. Financial Status

The project has used 37% of its budget of Tk. 391,300 (US \$26,087) as of the end of March 1980. Assuming the current strike which is curtailing collection of information is resolved in time to permit one additional month of fieldwork, there will be a surplus of Tk. 33,950 (US \$2,263) at the anticipated completion of the project in August 1980.

5. Future CDC Involvement

A trip to Bangladesh in August 1980 is anticipated to review coding procedures, to debrief field teams and the physicians who investigate each death, and to supervise the transfer of data from diskette to tape and to bring the tape back to the U.S. for analysis. An additional visit will be necessary to present the results of the study and discuss their implications. This visit will probably be in November 1980.

B. Investigation of Alleged Sterilization Deaths

1. Background of request for assistance

The Bangladesh government instituted a surveillance system for reporting deaths associated with sterilizations in 1978. Early in 1980, this system reported several deaths which were attributed to respiratory arrest. News of these deaths was reported by a chain of people, culminating with informal consultation with an anesthesiologist in the United States. The anesthesiologist made several recommendations for changes in the program to Dr. Coke McCord, the Medical Advisor to the United Nations Family Planning Association in Dacca. Dr. McCord forwarded those comments to AID Dacca and the Bangladeshi government and expressed concern over the possibility that simple steps could be taken to reduce or eliminate future deaths. AID/Dacca subsequently cabled the Center for Disease Control for assistance in investigating the deaths and in evaluating the sterilization program in Bangladesh.

2. Sterilization background

The facilities, equipment, and personnel at each center performing sterilizations in Bangladesh varies greatly. There are, however, common features which I have observed at the forty or so facilities I have visited and the approximately thirty tubectomies I have witnessed and facts I have ascertained by review of data at sterilization centers and from the Prospective Study of Sterilization (PSS). Review of that experience will provide the reader with a perspective on sterilization in Bangladesh.

A person seeking sterilization at centers which perform a high volume of sterilizations is interviewed by a trained assistant to be sure they understand the operation. At centers which do fewer procedures, a nurse or a clerk may serve the same function. A woman then generally has laboratory work performed; PSS records indicate this is nearly always hemoglobin or hematocrit and urinalysis for glucose and albumin. A brief physical examination, including pelvic, is performed. The surgeon then proceeds to the operating room, which might range

from a clean, well-equipped suite with several tables to a dusty back room lit by open windows with only the barest supply of drugs and instruments and which utilize a desk or board as an operating table. The physicians I spoke with indicated that men generally receive only a local anesthetic and no sedatives. Women receive a standard regimen of 100 mg. of pethidine (meperidine, Demerol) IV, 50 mg. of promethazine (Phenergan) IV, and 10 mg. of diazepam (Seduxen, Valium) IV just before the operation. Usually this regimen is administered regardless of weight (the average Bangladesh tubectomy client weighs 88 pounds²), but in several centers I noted the pethidine was decreased by 25 or 50 mg. for low weight. Sedation seemed to be considered sufficient when a woman showed no movement during the operation; if she did, the usual solution was to administer another 10 mg. of diazepam IV. The pethidine and promethazine are manufactured in Bangladesh, and the diazepam (Seduxen) is manufactured in Hungary. Several physicians have complained over suspected varying concentrations of drugs based on widely varying responses. My observation is that the standard regimen produces an effective sedation. I observed three brief (20-30 sec) episodes of respiratory arrest which resolved spontaneously, all of which went unnoticed by operating room personnel. The operation itself generally takes 5-10 minutes and is skillfully performed by surgeons who generally are very experienced. The woman is then brought into a recovery room which might range from a mat on the floor where she lays motionless and unobserved for several hours to a bed with somebody always in attendance. Men are sent home following the procedure, but women are nearly always kept overnight. Both are given a supply of penicillin or tetracycline; a review of 300 PSS charts indicates penicillin is given out twice as often as tetracycline, and my discussions with physicians indicate they give out whichever one of the drugs is on hand.

Personnel including physicians in the sterilization centers I visited do not know the contraindications and side effects of the drugs they use. For example, although most physicians were aware that penicillin could cause allergic reactions (none knew how frequently except that they were very rare), but few could cite either a contraindication or a bad side effect for tetracycline. About half the physicians I spoke with were unsure which emergency drugs to administer if respiratory or cardiac arrest occurred.

²Average weight of 250 randomly selected tubal ligation patients from Khulna clinic of Bangladesh Association for Voluntary Sterilization

Medical records of each procedure vary greatly. The largest centers keep excellent records detailing pre-, intra-, and postoperative condition, risk factors, and a thorough physical examination. The smallest, however, keep only a record of the person's name, date of procedure, and incentive paid. In general, records consisted of name, date of procedure, lab work, and incentive received. Records of number of procedures are kept by each center. Indications or morbidity rates are available only at the largest centers and are not reported to the government. No physician was able to compare their complication rate with other centers. Fatal cases associated with sterilization are reported by the district official.

3. Results

I reviewed reports of deaths attributed to sterilization collected by the Directorate of Family Planning and Population Control Division. When a death occurs, the Directorate is notified by cable, and reports are generally collected from the physician responsible for the patient's care and others with firsthand knowledge of the circumstances surrounding the death. Appendix C is a line listing of all deaths I was able to identify from these records, including two deaths following sterilization procedures performed in late 1978. The listing also includes two additional deaths reported by the PSS. The deaths come primarily from two government lists: the first is a summary list of all deaths reported to the government, and the second is a list of deaths occurring in Dinajpur district in 1979 which was presumably used to compile the summary list. However, review of the Dinajpur list revealed three deaths which were not included in the summary list. I was not able to find similar lists from other districts so was not able to compare the reported deaths from other areas of the country for completeness. Details of each death were reviewed from all available reports, many of which conflicted. The line listing, including cause of death, represents my best judgement of the most plausible reported circumstances of each death.

Appendix D presents the temporal distribution of deaths which followed procedures performed during late 1978, 1979, and early 1980, with the two most common causes of death indicated. Five deaths in 1980 where the month of procedure is unknown are omitted. Appendix E lists the deaths by geographical area, year and cause of death, and Appendix F demonstrates their geographical distribution.

Appendix G shows the number of tubal ligations and vasectomies performed by month, the deaths which are believed to have been related to the procedures, and the death rates by month. Samples of drugs used in sterilizations were obtained from various sources in Bangladesh and analyzed in the United States. These results are presented in Appendix H.

4. Discussion

The epidemic curve (Appendix D) shows a clustering of deaths in summer of 1979 with a second peak in the first 2 months of 1980 (the only months for which 1980 data is presently available). Since the reports for 1980 are still largely incomplete, it is possible that these numbers may ultimately be much greater than this preliminary indication. There is also good reason to believe that the deaths summarized here represent underreporting of an unknown magnitude, since thorough review of the government reports available expanded the official government list by 20% for 1979, and the PSS added two deaths to the 12 for 1980 which had been collected by the government at the time of my review. In addition, the manifold problems of compiling and transmitting accurate data in a country with a primitive system of communications must be emphasized. Examination of alleged causes of death, which must also be cautiously interpreted since there were few clinical reports indicating how a cause of death was assigned, reveals the chief cause of death in 1979 to be tetanus (53% of 17 deaths where cause was assigned). The second most common cause was pulmonary embolism (12%), but both these pulmonary embolism diagnoses were made in the same district, both in Bangladesh Association for Voluntary Sterilization (BAVS) centers, and both determined by the same team of investigators. Reports of these investigators are not presently available. For 1980, approximately half the reported deaths do not yet have details known. Of the eight deaths where the cause of death is known, five (63%) are attributed to respiratory arrest. This is a striking change from the previous year when no respiratory deaths were recorded.

The analysis of samples of drugs used in sterilization shows good agreement with the indicated concentrations (Appendix H), failing to support the contention that marked variations in potency contributed to recent respiratory deaths. The evidence remains indirect, however, since the batch numbers of the drugs in use at the time the deaths occurred is not known.

The monthly tubal ligation death rate for 1979 (Appendix G) varies between 0 and 6.5 (all rates are per 10,000 procedures), with a rate for the year of 1.2. The preliminary rates for the first two months of 1980 are 1.1 and 2.5. Although there are no published mortality rates for sterilization in less advanced developing countries, Potts has estimated the rate at 5-102. By comparison, the death rate for the PSS so far is 11.5. The vasectomy death rate for 1979 was 2.0, as compared to Potts' estimates of 0.01 for less advanced developing countries³. I believe that these proportions should be considered minimum death rates because of the unknown magnitude of underreporting.

It is evident from this preliminary investigation that further work is necessary to be certain that the reported deaths are actually due to sterilization. For example, a death attributed to tetanus occurred only two days after the sterilization, and a death 159 days after the procedure was also attributed to the sterilization; the association in both cases must be suspect. More information is needed about the preoperative condition of the patients who died, especially with regard to demonstrated risk factors such as the recency of delivery of children and health status. It is also desirable to obtain information on tetanus immunization and use of tetanus immunoglobulin (called antitetanus serum, or ATS, in Bangladesh), age, parity, religion, socioeconomic status, surgeon's skill, type of sterilization procedure, and availability of resuscitation and other emergency equipment. More refined death rates could be calculated if the number of procedures performed by month were available for each district, information which I was not able to obtain. More information is needed on changes such as antibiotic and sedative usage which have occurred throughout the sterilization program. There is also a need for detailed field investigation of the deaths reported here, especially the recent ones, in addition to an effort to determine the completeness of reporting. Some of this needed information is being provided by ongoing PSS, but a field investigation by a team of persons with skills in epidemiology and operative sterilization is indicated.

5. Conclusion and Questions Raised

Although confirmation of much of the information in this investigation was not possible, it appears that men and women undergoing sterilization are dying due to problems which may be remediable. The following points should be considered:

³Male and Female Sterilization, Population Reports Special Topics Monograph No. 2, March 1978

- a. Should the regimen for preoperative sedatives be changed? The current combination of drugs seems to lead to a marked respiratory depression in addition to powerful sedation. In addition to consideration of giving some or all of the drugs intramuscularly, a simple, clear guide to drug dosage should be developed based on height and body build and distributed to all sterilization centers. Another important component is to educate surgeons to the dangers of using large doses of sedatives simply so that patient will not move during the procedure.
- b. Should prophylactic antibiotics continue to be used, and if so, which ones? Most importantly, clinicians must realize that the incidence of wound infection is directly related to the density of organisms at the time of wound closure⁴ and that chemoprophylaxis is not a substitute for good surgical technique and judgement.

Surgical wounds are classified into 4 categories according to the potential for complicating infections; clean (involving strict aseptic technique), clean-contaminated (involving entry to abdominal cavity or viscera that have resident microbiota), contaminated (fresh traumatic wounds, operations involving abdominal cavity or viscera in which contamination exceeds that which is usual (by U.S. standards)) and dirty (abscesses, traumatic wounds untreated for more than 4 hours, and procedures dealing with perforated viscera).

The incidence of infection without chemoprophylaxis is about 15-20% for contaminated surgical wounds, and about 10-15% of clean-contaminated surgical wounds⁵. Most of the procedures in Bangladesh would seem to fall into one of these categories, indicating a need for prophylaxis. Choice of antimicrobial agent should include these considerations;

1. Efficacy in preventing infection. The most significant pathogen based on review of deaths appears to be Clostridium tetani, and the organism most likely to cause infection in abdominal wounds in tubectomy patients is Staphylococcus⁶. Although

⁴Polk HC, Lopez-Mayor JF: Postoperative wound infection: a prospective study of determinant factors and prevention. *Surgery* 66:97, 1969

⁵Reviewed in Chapter II, "The Use and Abuse of Antibiotics," in American College of Surgeons, Manual on Control of Infection in Surgical Patients, J.B. Lipincott, 1976

⁶Altheimer WA, Alexander TW, in Sabiston DC (ed). Textbook of Surgery. Philadelphia, W.B. Saunders, 1977

penicillin is the drug of choice for treating infections due to C. tetani, it has never been demonstrated to be of prophylactic value⁷. One can also anticipate significant resistance to penicillin by Staphylococcus⁸, and tetracycline is only approximately 65% effective against these two organisms⁹.

2. Safety. The frequency and severity of side effects of each drug must be weighed against other drugs and criteria for use. Parenteral penicillin, for example, is associated with an anaphylactic response rate of up to 0.04%, with 10% of those responses being fatal. Thus, if the 135,000 people who were sterilized in Bangladesh in 1979 all received parenteral penicillin, 5-6 could be expected to die as a result. The frequency and severity of more common side effects such as gastrointestinal upset will also limit the effective use of the drug.
3. Cost. In a program this large, small unit differences are magnified many thousandfold, and price becomes even more important in the context of the nation's poverty. In addition, indirect costs such as work time lost due to side effects and distribution costs (for example, if one drug were to substitute for the two currently used) also need to be considered.

Simultaneous evaluation of these points in considering different regimens might best be performed using cost-effectiveness model.

- c. Should there be certain minimal emergency equipment available at each sterilization center? This might consist of a narcotic antagonist, an Ambu bag or airway for mouth-to-mouth resuscitation, and NaHCO³ to reverse the acidosis induced by cessation of respiration. Larger centers might be required to have additional equipment.
- d. Should further training be provided to physicians and paramedical workers in the pharmacology of commonly used drugs and cardiopulmonary resuscitation along with provisions for periodic training? A manual might be developed and distributed

⁷Rubbo, SD, New approach to tetanus prophylaxis. Lancet 2:449, 1966

⁸Kucers A, Bennett NM: Penicillin G. in The Use of Antibiotics, Philadelphia, J.P. Lipincott, 1979

⁹Kucers A, Bennett NM: Tetracycline. in The Use of Antibiotics, Philadelphia, J.P. Lipincott, 1979

describing the drugs regularly used, their contraindications, dosages, side effects, and means of reversing the effects of the drug. In addition, a concise guide to resuscitation could be provided along with a wall chart. A regular schedule for recurrent training could be established to insure competency in emergency procedures.

- e. Should the surveillance system for deaths associated with sterilization be improved so that immediate, reliable information can be continually monitored?

Sterilization is probably the most acceptable and effective technique presently available to help control the population of Bangladesh, but a small number of unnecessary deaths has the potential of severely impairing the effectiveness of the program. Careful monitoring is essential to insure rapid identification of problems so that corrective steps can be taken. A standard form for reporting each death might be developed along with guidelines establishing responsibility for initial reports of the death and for collecting relevant reports, preparing a summary, and forwarding the summary to Dacca. Maximum time for reporting a death might be established and enforced. A team of trained specialists could be made available to investigate each death in detail using standardized forms. A series of incentives might also be established to encourage timely reports of deaths as well as routine numbers of procedures.

- f. Should a system of performance reports to be established so that each center can compare its performance and is encouraged to share in the sense of accomplishment for the country's future? This might initially consist of six monthly and yearly reports of number of procedures performed (perhaps as a proportion of goals established) and death rate, along with the same information for other centers in the District and the entire program. The other centers being compared should not be specifically identified.

C. Seminar on Choosing the Number of Subjects for a Study.

At the request of Dr. K.M.S. Aziz, Scientific Director of the International Center for Diarrheal Disease Research, Bangladesh, I presented a seminar on how to decide the number of cases and controls which are necessary for a study. The ICDDR,B does many field studies which postulate a difference between a treatment and control groups, and because of Bangladesh's poverty, financial considerations may be critical to a study's design. The talk was aimed at helping provide guidelines to

plan a study which would be economical yet large enough to assure scientific validity. For the talk I used examples from ICDDR,B researchers, and a good deal of interest was reflected. In addition to leaving a set of the guidelines I developed, I arranged to send a copy of a paper being written covering the same area.

D. Work on Manuscripts Concerning Abortion in Bangladesh

In follow-up of work completed last year on a project to define the practice of abortion and its impact on the health of Bangladeshi women, Tony Measham and I refined manuscripts in progress and discussed our plans for their completion and submission.

E. Discussion with International Planned Parenthood Federation

In London, I met with Pramilla Senanayake, M.D., of IPPF. We discussed my work in Bangladesh as well as the questions it raises and how changes might be implemented. She had the excellent suggestion that a good way might be to sponsor a national conference on sterilization in Bangladesh. We estimate such a conference would cost approximately \$50,000. She indicated that IPPF may be able to help underwrite such a meeting.

F. Discussions with Peter Layde, M.D.

Peter and I reviewed a paper being written regarding the reliability of retrospective data collection and discussed the problem of epidemiologic methodology described below.

G. Discussions with Ken Rothman and Olli Miettinen.

We discussed the question of whether a confidence interval which encompasses a relative risk of 1.0 indicates a "negative" study and whether the number of subjects in a study affects this interpretation. In particular, how does beta error (the chance of a "false negative" study which might be due to too few subjects) relate to the use of confidence intervals? The resolution seems to be in considering a study as either positive, negative, or indeterminate (an "agnostic" study, in Miettinen's words), in contrast to the classical statistical approach of classifying a study as either positive or negative.

Michael J. Rosenberg

Michael J. Rosenberg, M.D.

APPENDIX A
Information Collected 15 February - 14 April, 1980
Prospective Study of Sterilization

<u>District</u>	<u>Number of Procedures</u>			
	-----Tubal Ligation-----		----- Vasectomy -----	
	Form 1	Form 1+2	Form 1	Form 1+2
Rangpur	98	297	3	16
Bogra	277	214	70	31
Khulna	388	260	23	16
Dacca	48	358	0	31
Mymensingh	123	217	0	1
Chittagong	135	204	5	9
	-----	-----	-----	-----
Total	1019	1550	101	104

Total Tubal Ligations: $1019 + 1550 = 2569$

Total Vasectomies: $101 + 104 = 205$

Total procedures: 2774

NOTES:

Form 1 = Intrahospital information

Form 2 = Followup information

APPENDIX B
Emergency Equipment on Hand
Centers Performing Sterilizations Included in the
Prospective Study of Sterilization
Bangladesh, 1980
(n=37)

<u>Item</u>	<u>%</u>
Instruments for laparotomy	89
Steroids (for parenteral use)	87
Epinephrine (for injection)	59
Intravenous fluids & administration set	51
Narcotic antagonist	43
Oxygen & mask	38
Emergency airway or Ambu bag	35
Motor vehicle for emergency evacuation	12
Laryngoscope + endotracheal tube	6

APPENDIX C
ALLEGED STERILIZATION DEATHS
Bangladesh, 1979-80

Sex	Procedure				Death		Alleged Cause	Comments
	Date	City	Division	Type Facility	Date	Interval Since Operation (days)		
1. F	30 Nov 78	Ketgaon	Dinajpur	THC	8 Dec 78	9	Peritonitis 2° perforated ulcer	Prior history of peptic ulcer
2. F	25 Dec 78	Thakurgaon	Dinajpur	SDH	3 Jan 79	7	Tetanus	
3. F		Ghasipara	Dinajpur	BAVS	30 Mar 79		Tetanus	
4. F	19 Apr 79	Hakimpur	Dinajpur	BAV	19 Apr 79	0	Anaphylactic shock	Died before procedure
5. F	30 May 79	Bramanbaria	Comilla	MCH	30 May 79	0	Shock	
6. M	28 May 79	Pirganj	Dinajpur	RHC	9 Jun 79	11	Tetanus	
7. F	19 May 79	Jagannathpur	Dinajpur	SDH	31 May 79	12	Tetanus	
8. F	5 Jun 79	Chibandha	Rangpur	BAVS	5 Jun 79	0	Heat stroke	Died 4 hours after operation
9. F	5 Jun 79	Tongi	Dacca	BAVS	5 Jun 79	0	Pulmonary embolism	
10. F	5 Jun 79	Thakurgaon	Dinajpur	RHC	17 Jul 79	42	Tetanus	Same surgeon and center as #15
11. F	5 Jun 79	Thakurgaon	Dinajpur	MCH	19 Nov 79	159	"Postoperative complication"	
12. F	14 Jun 79	Parbatipur	Dinajpur	RHC	15 Jun 79	1	Tetanus Heart failure	
13. F		Palash	Dacca	BAVS	27 Jun 79		Pulmonary embolism	

APPENDIX C
ALLEGED STERILIZATION DEATHS
Bangladesh, 1979-80

Sex	Procedure				Death		Comments	
	Date	City	Division	Type Facility	Date	Interval Since Operation (days)		Alleged Cause
14. M	23 Jun 79	Patnitela	Rajshahi	RHC	4 Jul 79	14		
15. M	2 Jul 79	Pirgonj	Dinajpur	RHC	16 Jul 79	14	Tetanus	Same surgeon and center as #10
16. M	2 Jul 79	Thakurgaon	Dinajpur		17 Jul 79	15	Tetanus	
17. F	3 Jul 79	Pirgonj	Dinajpur	RHC	14 Jul 79	11	Tetanus	
18. F	25 Jul 79	Marichbunia	Patuakhali	Hospital	27 Jul 79	2	Tetanus	
19. F	1 Aug 79	Bogra	Bogra	BPPA	1 Aug 79	0	Suffocation due to roundworms	
20. M	12 Nov 79	Ranisankail	Dinajpur	Dispensary	19 Nov 79	7	Bleeding	
21. M	13 Jan 80	Tahirpur	Sylhet	MCWC	15 Jan 80	2	Hematoma, infection	
22. F	17 Jan 80	Sree Bandar	Dinajpur	MCH	21 Jan 80	4	Heart failure	
23. F	24 Jan 80	Mirajpur	Tangail	Hospital	24 Jan 80	0	Respiratory arrest	
24. F	7 Feb 80	Baidyer Bazar	Dacca	MCH	7 Feb 80	0	Respiratory arrest	Said to be severely anemic; died before op'n
25. F	12 Feb 80	Fengaha	Faridp	Hospital	12 Feb 80	0		
26. F	17 Feb 80	Jaylebpur	Dacca	LWC	17 Feb 80	0	Respiratory arrest	
27. F	25 Feb 80	Gabrali	Bogra	RHC	25 Feb 80	0		Died during op'n
28. F	26 Feb	Issharedi	Pabna	Hospital	26 Feb 80	0		Died during op'n

18

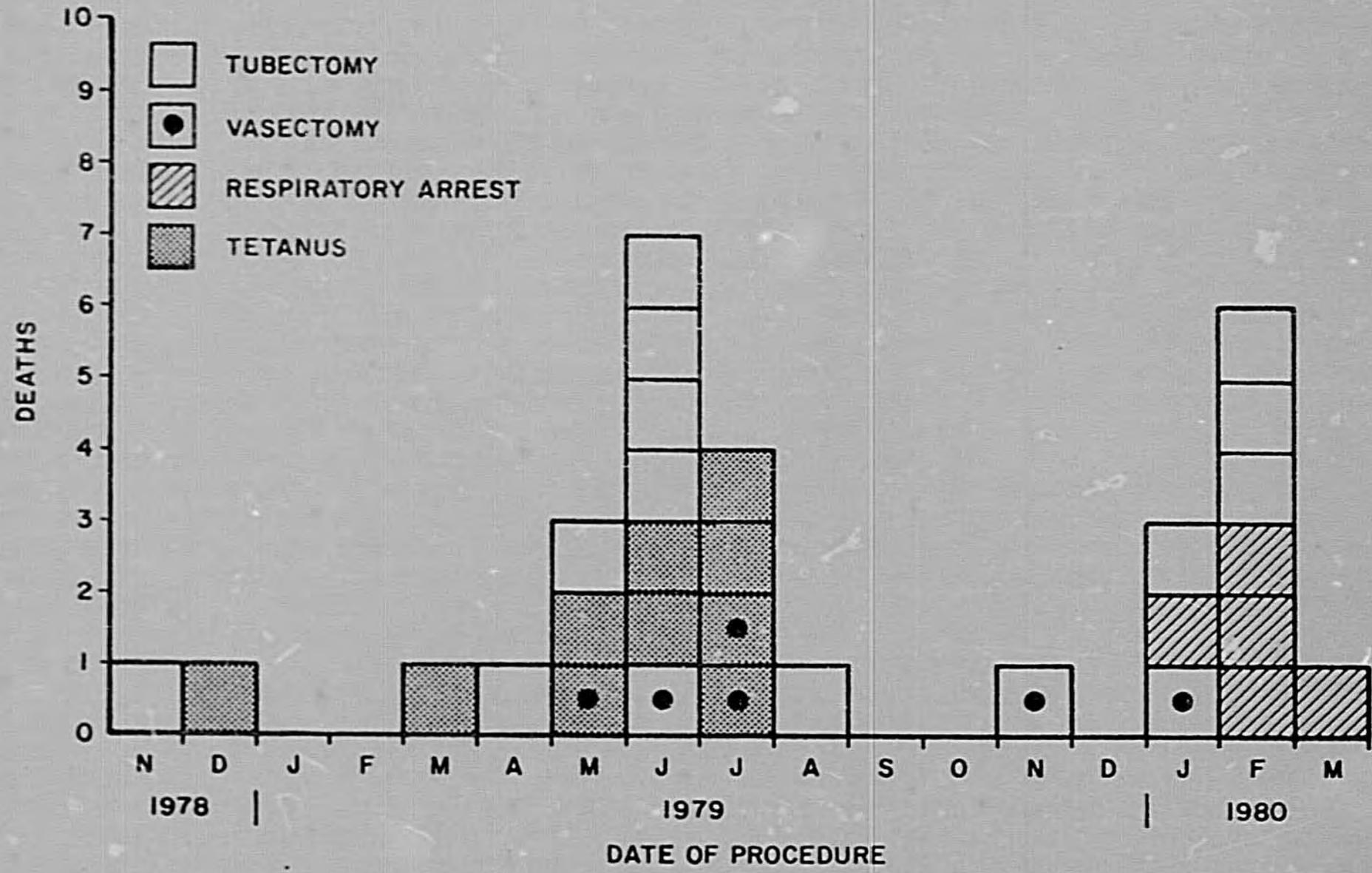
APPENDIX C
ALLEGED STERILIZATION DEATHS
Bangladesh, 1979-80

Sex	Procedure			Death			Comments
	Date	City	Division	Type Facility	Date	Interval Since Operation (days)	
29.			Mymensingh	MCH	10 Mar 80		
30. F			Mymensingh				
31. F			Dinajpur				
32. M			Mymensingh				Infection and other complications
33. M			Mymensingh				
34. F	21 Feb 80	Bageehat	Khulna	MCH	21 Feb 80	0	Respiratory arrest Detected by PSS
35. F	10 Mar 80	Kishoreganj	Rangpur	MCH	10 Mar 80	0	Respiratory arrest Detected by PSS

Abbreviations

BAVS - Bangladesh Association for Voluntary Sterilization
 BFPA - Bangladesh Family Planning Association
 LWC - Labor Welfare Center
 MCH - Maternal-Child Health Center
 MCWC - Maternal-Child Welfare Center
 PSS - Prospective Study of Sterilization (in progress)
 RHC - Regional Health Center
 SDH - Subdivisional Hospital
 THC - Thana Health Complex

APPENDIX D
 Deaths Allegedly due to Sterilization, by Month and Type
 of Procedure and by Presumptive Cause of Death
 Bangladesh, November 1978-
 March 1980

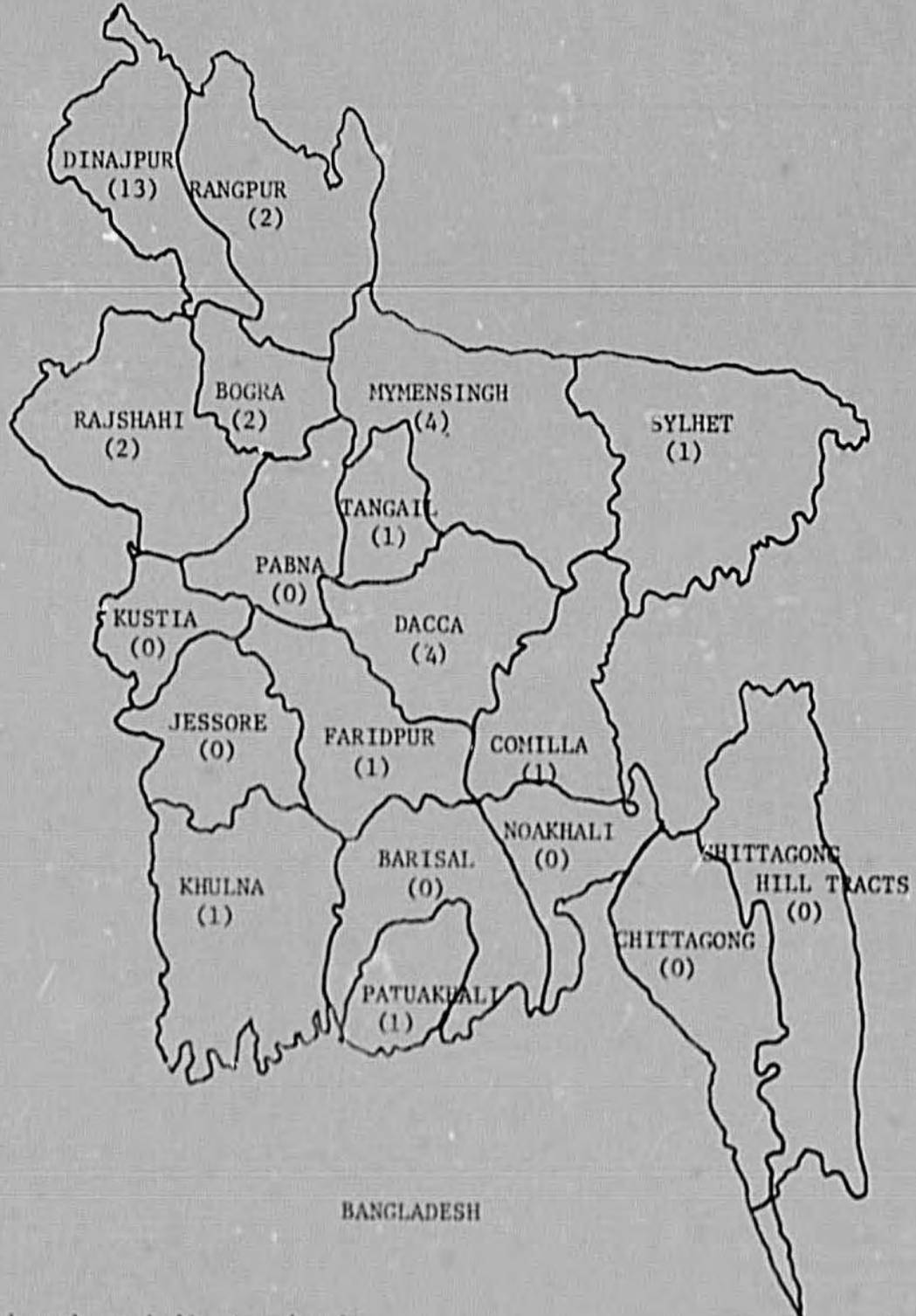


20

APPENDIX E
Alleged Sterilization Deaths, by Division,
Cause, and Date of Procedure

	-----1979-----										-----1980-----				
	Tetanus	Unknown	Pulmonary embolism	Heat Stroke	Anaphylactic Stroke	Shock	Bleeding	Parasites	Postoperative complications	TOTAL	Unknown	Respiratory arrest	Infection	Heart Failure	TOTAL
Dinajpur	1	.	1	.	1	11	1	.	.	1	2
Rangpur	1	1	.	1	.	.	1
Bogra
Pabna
Tangail	1	.	.	1
Mymensingh	3	.	1	.	4
Sylhet	1	.	1
Kustia
Dacca	.	2	2	.	2	.	.	2
Jessore
Faridpur	1	.	.	.	1
Comilla	1	.	.	.	1
Khulna	1	.	.	1
Barisal
Noakhali
Patuakhali	1	1
Chittagong
Chittagong Hill Tracts
TOTAL	9	1	2	1	1	1	1	1	1	18	7	5	2	1	15

APPENDIX F
GEOGRAPHICAL DISTRIBUTION OF ALLEGED
STERILIZATION DEATHS,
Bangladesh, January 1979-March 1980



BANGLADESH

Circled numbers indicates deaths

APPENDIX G

Alleged Sterilization Deaths,
Number of Procedures and Death Rates by Month
Bangladesh, January 1979-March 1980

Date of Procedure	No. Procedures		Deaths		Vasectomy	
	Tubal Ligation	Vasectomy	No.	Rate ¹	No.	Rate ¹
1979						
January	2,816	536				
February	2,053	376				
March	7,578	1,189	1	1.3		
April	7,198	1,190	1	1.4		
May	3,471	1,729	2	2.4	1	5.8
June	9,297	2,391	6	6.5	1	4.2
July	11,236	2,802	2	1.8	2	7.1
August	4,424	1,369	1	2.3		
September	12,872	3,018				
October	16,961	6,057				
November	14,260	3,210				3.1
December	13,246	1,442				
Total	110,462	25,329	13	1.2	5	2.0

For 1979, death rate = $\frac{\text{Total no. deaths}}{\text{Total no. procedures}} = \frac{18}{135,791} = 1.3^1$

1980 ²	January	17,973	1,744	2	1.1	1	5.7
	February	24,370	2,340	6	2.5		
	March	22,156	2,440				

¹per 10,000 procedures.

²1980 Deaths do not include 5 deaths where data of procedure is unknown

Source: Directorate of Family Planning and Population Control Division,
People's Republic of Bangladesh.

APPENDIX H
Analysis of Samples of Drugs Used in Sterilizations
Bangladesh, 1960

Source in Bangladesh	Drug	Manufacturer	No. of Vials	Concentration On Label	Other Identification	Drugs found and concentration (as percent of labelled concentration) ^{1, 2, 3}
Public Sterilization Center, Rangpur	Valium	Hoffmann-La Roche	1	10 mg/2 ml	Exp. 6-80, B3915	Valium, 100%
	Phenergan	Bangladesh Pharmaceutical Industry Ltd.	1	50 mg/2 ml	Lot 198	Phenergan, 100.4%
	Atropine	KDH Lab Ltd. Dacca	1	1/100 gr	Batch No. 19	Atropine, 104%
	Pethidine HCL	Anino Ltd.	2	50 mg/1 ml	7/3	Pethidine, 101.0%
Purchased at Pharmacy in Dacca	Seduxen	Richter	2	10 mg/2 ml	77621.1075	Seduxen, 100%; lidocaine, 3.5 mg.; 3 unknown drugs
	Pethidine HCL	Jayson Pharmaceuticals, Ltd, Dacca	1	100 mg in 2cc	Batch No. 219	Pethidine, 104.5%
Gov't Stock in Dacca (Obtained from private physician)	Seduxen	Richter	1	10 mg/2 ml	42879.1173	Seduxen, 90%; lidocaine, 2.9 mg.; 3 unknown drugs
	Pethidine	Jayson Pharmaceuticals,	1	100 mg in 2cc	Batch No. 237	Pethidine, 98.7%
	Pethidine HCL	S.P. Co.	1	100 mg/2 ml	Batch 6C07	Pethidine, 98.6%
	Pethidine HCL	Vijay Chandra	1	100 mg/2 ml		Pethidine, 103.6%
	Pethidine HCL		1	100 mg	DMI No. 20	Pethidine, 105.7%
	Unmarked		1		(said to be Pethidine)	Pethidine, 102.8 mg/2cc
Gov't Sterilization Program Storehouse	Phenergan	Bangladesh Pharmaceutical Industry Ltd.	5	50 mg/2 ml	Lot 214	Phenergan, 100.2%
	Seduxen	Richter	5	10 mg/2 ml	38704.0178	Seduxen, 94%; lidocaine, 3.1 mg.; 3 unknown drugs
	Atropine	KDH Lab Ltd. Dacca	5	1/100 gr	Batch No. 23	Atropine, 102%
	Pethidine	Jayson Pharmaceuticals, Ltd., Dacca	4	100 mg	Batch No. 237	Pethidine, 98.7%

- Notes:
1. Determined by chromatography by the United States Food and Drug Administration
 2. United States Pharmaceutical standards (U.S.P.) for concentrations of pethidine (meperidine) is 95-105%; for diazepam (Seduxen, Valium) and promethazine (Phenergan), the standards were not known at the time this list was compiled
 3. Where multiple vials were available, the concentration was determined of only one of the samples.

24