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PROJECT SUMMARY

Project Title :	Reversible Sterilization
Proposed Contractor :	University of North Carolina Chapel Hill, North Carolina
Principal Investigator:	J. F. Hulka, M.D., Associate Director Carolina Population Center
Duration :	Three years, beginning approx. December 1968
Estimated Cost:	(a) Total - $254,648 (b) FY 69 - 87,220 (c) FY 70 - 89,279 (d) FY 71 - 78,149
Proposed FY 69 Funding :	$150,000 (approx. 18 months)
Action Officer:	George Contis, M.D., NESA/PFP

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1. Background

Sterilization, especially vasectomy, is being used increasingly as a complement to other contraceptive methods to reduce fertility. In India, for example, sterilizations have been used as the major method of birth control since 1956. The monthly sterilizations for September 1968 were three times the number of IUD insertions and brought the total number of sterilizations to about 4.6 million. Government officials have been giving primary emphasis to this method of birth control since growing acceptance is crucial to the Indian family planning program. Sterilizations are also used to a lesser extent in Pakistan, Nepal and other countries.

There are two limitations to the increased acceptance of sterilizations as presently performed. One is that fairly skilled surgeons are required for the operations -- a restricting factor in countries where medical manpower is scarce. The other is a psychological factor relating to the irreversibility of the operations. Traditional sterilizations involve the excision and tying off of the vas deferens or fallopian tubes, and reversibility is accomplished only by difficult surgery which is not always successful. A technique which is more

readily reversible, and can be performed by average doctors within a minimum of discomfort, will attract more people to this method of controlling reproduction.

2. Description of Proposed Project

This project proposes to continue investigating simplified surgical techniques which would minimize the time and surgical skill required to perform the operations and would reduce complications such as hematoma, sperm granuloma, scrotal abscess, etc.

Research on two types of reversible methods is proposed. One method calls for an evaluation of a tantalum clip which would serve as an occluding device for the vas deferens and fallopian tubes; preliminary animal research has already been done, and human research on 100 male volunteers is now underway in India. Animal studies thus far indicate that sterilization by this method is effective and is more readily reversible because the vas deferens and fallopian tubes are not excised or tied.

The second technique involves the development of a plastic occluding device. Preliminary discussions with an experienced plastic developer and manufacturer in the U.S. indicate that these devices could be designed to permit reversibility by means of a built-in valve structure. The devices would be inserted into the vas and tubes by simple surgery.

Both of these reversible techniques would require the development of a laparoscopy approach to the uterine salpinx to make widespread application of the clip or device practical for female sterilization. Studies are now being made to develop this approach, which would reduce the period of hospitalization and not require general anesthesia. This method introduces air into the abdomen and creates a negative pressure, distending the abdomen. A laparoscope would then be inserted and the abdominal contents examined. Experiments would be performed on laparoscopy with sedation and local anesthesia only, with general anesthesia available. The actual sterilization process would then require a stab incision during laparoscopy to permit the introduction of an instrument for placing the clip or device close to the uterotubal junction. If animal studies indicate its feasibility, the laparoscopy approach would enable the sterilization process to be conducted in an out-patient clinic.

Both techniques would be evaluated in terms of blood hormone levels, sperm count, and atrophic changes within animals and people. Possible psychological effects of humans would also be assessed. The animal research, laboratory studies, and clinical studies on female sterilization would be conducted at the University of North Carolina. The clinical studies on males would be done at the Institute of Rural Health and Family Planning in Gandhigram, India.

In summary, the major purposes of this project are:

a. To test the effectiveness, ease of application, and psychological acceptance of the tantalum clip and plastic occluding device for sterilizations, particularly vasectomies, vis-a-vis conventional techniques by continuing research on animals and on human volunteers.

b. To experiment with laparoscopy under sedation and local anesthesia as a means of making clip and plastic device occlusion in females a simpler procedure.

c. To evaluate the effectiveness of the reversible sterilization techniques in terms of subsequent fertility and in terms of physiological and psychological changes.

3. Significance of Project to A.I.D. Objectives

A.I.D.'s highest priority is to assist nations in achieving a better balance between population and resources so that economic and social development may take place. One means of achieving this goal is by reduced fertility. Fertility reduction must be promoted by making a variety of acceptable birth control methods easily available. Many couples desire greater protection, more freedom, and fewer side effects than are afforded by the IUD, pills, or conventional contraceptive methods. Sterilization fulfills these criteria except for the aspect of its possible irreversibility. Reversible sterilization techniques would be theoretically more efficient in preventing unwanted births, would not require sustained motivation on the part of the contraceptor, and would remove the psychological barriers to surgical sterilization techniques.

Support of this research would be consistent with A.I.D.'s desire to seek alternative or additional approaches to family planning and population control. Inasmuch as the extent of anticipated reduction in fertility from other approaches -- e.g., delaying onset of reproduction, reduction of illegitimacy, provision of later employment opportunities for young women, sex education in school systems, tax incentives or disincentives, etc. -- is unknown, the possible addition of reversible sterilization techniques may assist in reducing fertility levels and hence appears to be a logical proposal.

4. Relevance of Project to Existing Knowledge

The approach to sterilizations proposed in this study is a unique modification of existing techniques. It will use a surgical clip which has been demonstrated to be useful in other fields of surgery.

The plastic device is a new approach to sterilization but is not a radical or dangerous departure from existing methods.

The project should have special interest in major areas of the world such as India and Pakistan where sterilization techniques are included in government programs for population control. Projection of the methodology so as to permit reversible sterilization could be a significant step in any program that seeks substantial population control measures.

5. Description and Evaluation of Methodology

Research on the reversible sterilization techniques will be conducted in two overlapping stages. During Phase I, the tantalum clip will be used as an occluding device on the vas deferens and fallopian tubes of animals. When the animal data warrant, this approach will be used in a prospective study of 100 male volunteers undergoing vasectomy in India (scheduled to begin in October 1968). Also during Phase I, a laparoscopy approach to the fallopian tubes, which does not require general anesthesia or prolonged hospitalization, will be developed.

During Phase II, the plastic occluding device will be designed, produced, and tested at the pre-clinical and clinical levels. Clinical research, laboratory analysis, follow-up, and evaluation of the clip method will continue.

A Phase III follow-up operation will specifically include the incidence of successful impregnation after reversal of sterilization. Another follow-up technique involves examination of the semen of the male after the reversed sterilization has been effected.

6. Evaluation of Research Competence of Investigators

The principal investigator of this project will be J. F. Hulka, M.D., who holds appointments in the University of North Carolina Medical School's Department of Obstetrics-Gynecology, in the Department of Maternal and Child Health in the School of Public Health, and as Associate Director of the Carolina Population Center. His major interest is reproductive biology. Recently, he has done research on the antigenicity of the trophoblast to provide clues about transplant rejection.

Dr. Pralhad Jhaver is a private surgeon at the City Hospital in Indore, Madhya Pradesh, who will serve as principal consultant for the project. He will direct the clinical studies on males in India. Dr. Jhaver has been involved in clinical research on male sterilization techniques for several years, having developed a single incision sterilization operation. He has performed over 10,000 traditional sterilizations.

7. Appraisal of Research Resources and Budget

Research resources at the University of North Carolina and the Institute of Rural Health and Family Planning at Gandhigram are well suited for the current project. Animal and laboratory facilities are more than adequate

at the University of North Carolina, and Medical School professors have agreed to serve as consultants for various phases of the research, e.g., evaluation and hormonal and histologic changes before and after occlusion. Dr. Ranganathan, Director of the Institute of Rural Health and Family Planning at Gandhigram, spent a year at the Carolina Population Center and is in an excellent position to provide follow-up on the Indian patients.

The budget appears reasonable with respect to salaries and additional equipment requested. The principal budgetary items are indicated in the attached summary; a more detailed breakdown is provided in the proposal.

8. Technical and Scientific Review of the Project

a. Within A.I.D.: Both the NESA Bureau and the Population Service, WOH, have reviewed the research proposal and have indicated strong interest in it. The project also has been reviewed in detail by the Deputy Assistant Administrator/NESA and the Bureau's top-echelon technical, operational and planning staff. The results have been uniformly favorable.

b. Outside consultation: Dr. Moye W. Freymann, Director of the Carolina Population Center and consultant to the NESA Bureau, has reviewed the proposed research and believes that it has great promise for family planning program development.

9. Summary Evaluation

There is considerable urgency for the approval of this project. Dr. Jhaver, the principal consultant, recently returned to India to conduct experiments with the tantalum clip on 100 male volunteers (who planned to undergo traditional sterilization) at the Institute of Rural Health and Family Planning at Gandhigram. Dr. Jhaver should finish sterilizing 200 men -- a control group of 100 and an experimental group of 100 -- by December of this year. If A.I.D. funds are not forthcoming soon, the research will have to be discontinued or slowed down to match available funds.

We believe that this project may yield high pay-offs for the investment involved. Improved methods of sterilization, which are simpler for both doctors and patients and which are emotionally appealing, would have applicability throughout the world. In countries where sterilization is already an important method, such improvements would provide even more people with a realistic choice for a suitable contraceptive method. We heartily support this research.

Attachment: Proposed Budget

NESA/PFP:STCrawford:10-24-68
WOH/PS :MDLieberman:10-14-68

Attachment

Proposed Budget

	FY 1969	FY 1970	FY 1971
1. Salaries	$52,380	$44,447	$46,305
2. Equipment	4,000	13,500	
3. Supplies	9,700	9,700	9,700
4. Travel	12,100	12,100	12,100
5. Indirect costs	9,040	9,532	10,044
Total	$87,220	$89,279	$78,149