AGENCY FOR INTERNATIONAL DEVELOPMENT
WASHINGTON, D. C. 20523
BIBLIOGRAPHIC INPUT SHEET

FOR AID USE ONLY
Batch 98

1. SUBJECT CLASSIFICATION
A. PRIMARY: Population — PC00-0000-0000
B. SECONDARY: Family planning

2. TITLE AND SUBTITLE
Surgical and engineering research on means of fertility control; Project I: New and improved methods for postconception fertility control. Final report

3. AUTHOR(S)
(101) Battelle Memorial Inst., Columbus,Ohio

4. DOCUMENT DATE	5. NUMBER OF PAGES	6. ARC NUMBER
1979	54p.	ARC

7. REFERENCE ORGANIZATION NAME AND ADDRESS
Battelle

8. SUPPLEMENTARY NOTES (Sponsoring Organization, Publishers, Availability)
(Final report)

9. ABSTRACT

10. CONTROL NUMBER
PN-AAG-385

11. PRICE OF DOCUMENT

12. DESCRIPTORS
Medical equipment
Surgical instruments
Abortion
Pregnancy

13. PROJECT NUMBER
932170530

14. CONTRACT NUMBER
AID/csd-3152

15. TYPE OF DOCUMENT

AID 590-1 (4-74)

1a

FINAL REPORT

Surgical and Engineering Research on Means of Fertility Control

Project I: New and Improved Methods for Postconception Fertility Control

January 1979

Prepared for
Agency for International Development
under Contract AID/csd-3152

Battelle
Pacific Northwest Laboratories

LEGAL NOTICE

This report was prepared by Battelle as an account of sponsored research activities. Neither Sponsor nor Battelle nor any person acting on behalf of either:

MAKES ANY WARRANTY OR REPRESENTATION, EXPRESS OR IMPLIED, with respect to the accuracy, completeness, or usefulness of the information contained in this report, or that the use of any information, apparatus, process, or composition disclosed in this report may not infringe privately owned rights; or

Assumes any liabilities with respect to the use of, or for damages resulting from the use of, any information, apparatus, process, or composition disclosed in this report.

PROJECT I

AID/csd-3152

NEW AND IMPROVED METHODS FOR POSTCONCEPTION FERTILITY CONTROL

Project Manager: John F. Williford
Principal Investigators: Loyd L. King
Richard D. Tokarz

Contributors:

Richard L. Bernstine
J. Leland Daniel
Gordon W. Duncan
James C. Dunn
Thomas M. Fish
Lorraine O. Foley
N. Ross Gordon
James H. Jarrett
Roy C. Kelley
Max R. Kreiter
Brent R. Lower
Robin N. Madison
Denis J. Prager
Wayne G. Riches
W. Eugene Skiens
John D. Smith
Robert G. Wheeler
Genevieve E. Wilson

Technical Advisors:

Benjamin Branch
William E. Brenner
Michael S. Burnhill
John T. Conrad
H. Robert Holtrop
Richard M. Soderstrom
Philip G. Stubblefield

Cooperating Institutions:

Johns Hopkins School of Medicine
International Fertility Research Program

BATTELLE
Pacific Northwest Laboratories
Richland, Washington 99352

1d

SUMMARY

This final report reviews significant accomplishments under AID/csd-3152, Project I, New and Improved Methods for Postconception Fertility Control.

Work is discussed under two main headings:

Historical Review of Vacuum Source Development

Historical Review of Ancillary Instruments and Other Activities

Accomplishments described herein include the following:

1. Development of an aspirating syringe and cannulae for early abortion, followed by international clinical testing, transfer of technology to U.S. and LDC makers, and widespread international use of the instrument in Asia, Latin America and Africa through activities of the International Fertility Research Program, the International Projects Assistance Services, International Planned Parenthood Federation, the Population Crisis Committee, The Pathfinder Fund and most recently the World Health Organization.

2. The development and field evaluation of hand-pumped aspiration equipment for uterine evacuation throughout the first trimester, transfer of technology, and clinical trials demonstrating safety and efficacy. The equipment is supplied by two U.S. makers, is being adopted by an LDC manufacturer, and is being procured and fielded by The Pathfinder Fund and the World Health Organization.

3. Large cannula, rotary handle and collection tubing designs were developed for 2nd trimester D&E, proven at Harvard Medical School, and are currently available from commercial suppliers.

4. Basic principles of mechanical dilation have been validated through collaboration with parallel research by Preterm Institute.

1a

5. New mechanisms underlying cervical dilation have been identified and open entirely new directions for future work.

6. Methods and materials have been established for preparation of elastic bands for female sterilization; the technology has been transferred to a Bombay manufacturer, and an indigenous product is now on the Indian market.

18.

CONTENTS

Summary iii
Introduction 1
Historical Review of Vacuum Source Development 3
Syringe-Type Aspirators 3
Negative Pressure Bottles 10
Hand-Powered Aspirator 13
Historical Review of Ancillary Instruments and Other Activities 25
Cannula Materials Studies 25
Comparative Cannula Pattern Studies 26
Cervical Dilation 27
Tenaculum Design 32
Large Cannula System 33
Transfer of Elastic Band Technology 35
Conclusions and Recommendations for Future Research and Development 37
Vacuum Equipment 38
Cannulae 39
Cervical Dilation 40
Clinical Studies 41
Summary Observation 41
References 42
Acknowledgements 44

19

INTRODUCTION

This final report summarizes the activities on efforts dating from 1972, and in consequence glosses over or omits work which led to dead ends or appeared to have little advantage over current art or work already underway by others. Such work has already been reported in detail in earlier progress reports.

By focusing our attention on those active elements of the research which have run throughout the project, our intent has been to place all of the more significant developments within one document of readable length.

The development with the largest international impact to date has been an effective and safe syringe aspirator for early pregnancy termination and diagnostic use. This instrument has undergone some modifications in design following its introduction into international trials beginning in 1974, following a moratorium of nearly two years on design changes. These have vastly improved durability of the instrument and accordingly benefited the economics of international use, particularly in LDCs.

The availability of the MR syringe, as it evolved from our studies, has had such an immense international impact (with at least 5 million procedures performed since 1974) that it has tended to overshadow other work and to some degree to delay clinical emphasis on other instruments. However, the technology is now well established for instruments to deliver care throughout the first trimester, and the importance of these developments will doubtless gain recognition with time as the World Health Organization, the International Fertility Research Program and others continue to build an international data base.

Some new directions remain to be taken, notably in the area of safe cervical dilation. Although our efforts, based on the current consensus on cervical tissue behavior, have not been successful, they have suggested new and important mechanisms for the dilation process.

New technology developed by the Battelle program has been transferred to both U.S. and LDC industry, and the major changes in provision of

uterine aspiration services worldwide would have been impossible without AID's support and Battelle's creative efforts.

HISTORICAL REVIEW OF VACUUM SOURCE DEVELOPMENT

Work began in earnest on Project I in 1972, following a series of site visits in the U.S. and a conference held in Seattle in December, 1971.[1] Emphasis was on the development of vacuum sources suitable for the LDC setting, considering both electrical and nonelectrical systems.

With electrical systems, attention was given to existing commercial units, and specifications relating to field conditions as well as functional characteristics were developed.[2] Under a subcontract with an independent testing company, candidate units were subjected to a series of tests under standard conditions, including high ambient temperatures and relative humidity. The best commercial aspirator was thus found and specific problems with this unit were identified and corrected. The Berkeley Bioengineering electrical aspirator subsequently became the primary research and service instrument distributed internationally by AID during the final year such activity was permitted by Congress.

In the category of nonelectrical sources, the picture was less promising, as no satisfactory commercial units could be identified. Accordingly, attention was focused on the creation of three new classes of nonelectrical aspirator, with increasing capacity to cope with increasing gestation:

- Syringe-type aspirators for very early MTP and diagnostic procedures
- Negative pressure bottles of greater capacity for use up to 9 or 10 weeks
- Hand-powered aspirators to deal with procedures through the first trimester

Some of the history and accomplishments with these instruments are discussed below, treating each separately.

SYRINGE-TYPE ASPIRATORS

Work on the syringe began shortly after the initial reports of clinical work with the original Karman design.[3] Little was known about

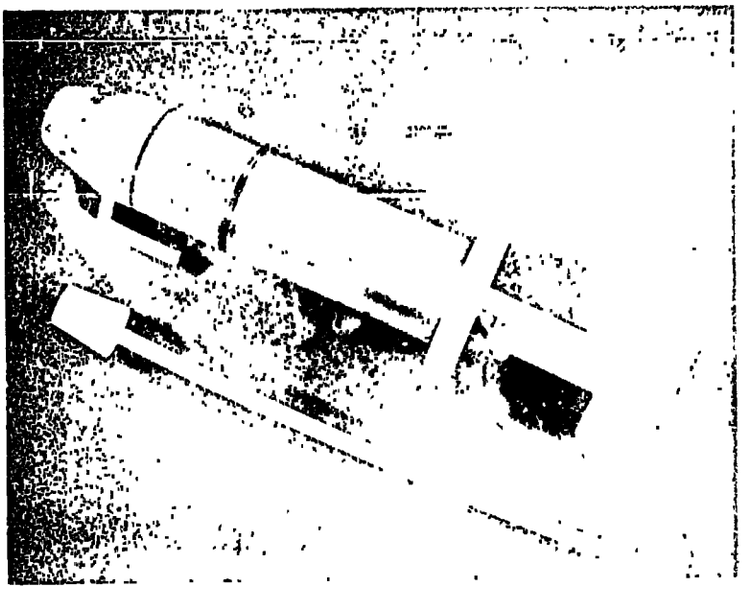
the requirements for such an instrument, and our Medical Advisory Committee defined the boundaries as they were perceived in 1972. These consisted of an increased capacity of 100cc or greater, improved piston locking, safety valving to preclude pressurization and a vacuum control valve to facilitate evacuation and conserve vacuum in use. A further condition was that the instrument should be made robust enough to provide prolonged field service of hundreds of cycles.

These boundaries were held to, and the syringe shown in Figure 1 was developed, using a novel rotary control valve design, replaceable seals and a ratchet-type, positively locking handle arrangement. Prototypes were assessed by clinical advisors and the status of the instrument was reviewed at a Medical Advisory Committee meeting in the spring of 1973.[4]

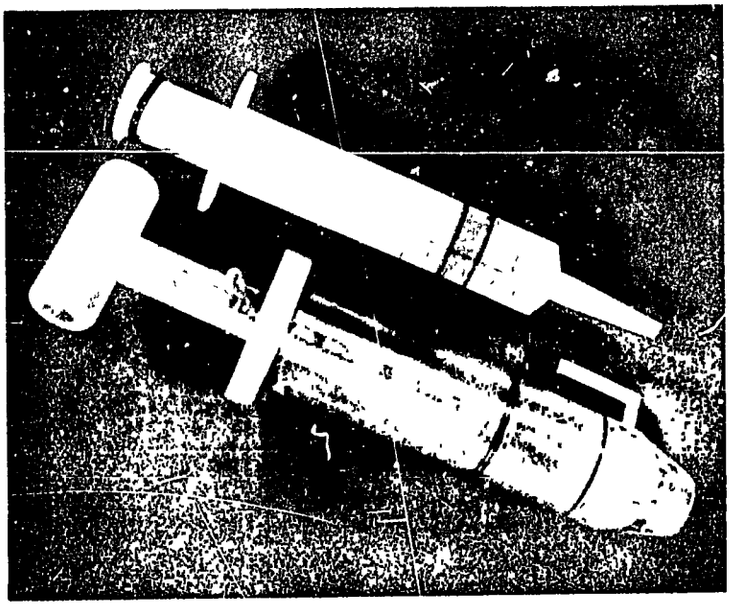
At this meeting the technical aspects were reviewed and the Medical Advisors and AID Technical Monitors agreed with us that the constraints should be modified to permit a solution structured around the readily available 50cc irrigation syringe, retaining some features of the prototype. Within a matter of weeks, an entirely new design was devised, prototypes made, and models submitted to clinical advisors for assessment. The first, hand-built model of the Battelle-modified Karman syringe is shown in Figure 2.

On our site visits to India in September, 1973, with the original prototypes we saw firsthand the extraordinary benefits of the design refinements on acceptability of the instrument to users and research contributors. The addition of the vacuum control valve liberated the user from evacuating the syringe while it was attached to the uterus, and, in combination with the improved handle, this spelled the difference between easy evacuation and inability to use the instrument.

Specifications and detailed designs were worked out for this instrument in 1973,[5] vendors were identified, and commercially made kits for early MTP were procured by AID. Under a separate contract, Battelle and the University of Hawaii conducted an international Menstrual

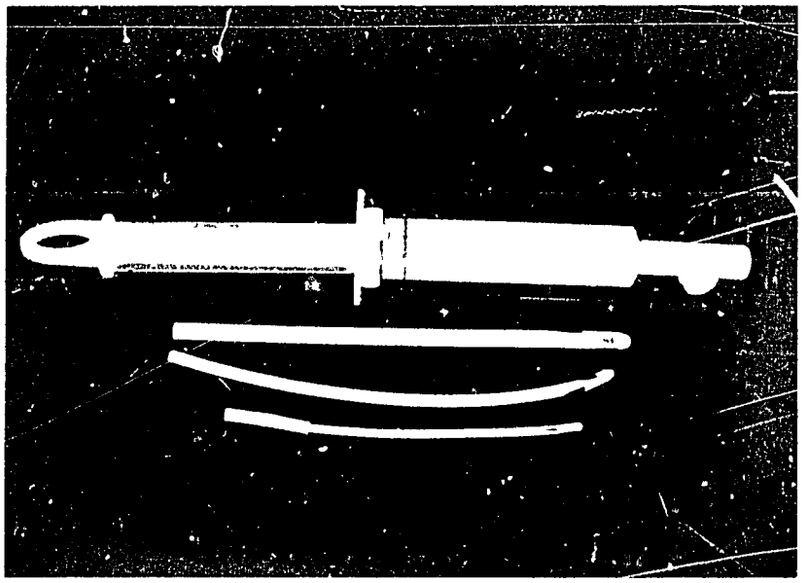


a) Model 300 Syringe with Cannula and Adapter

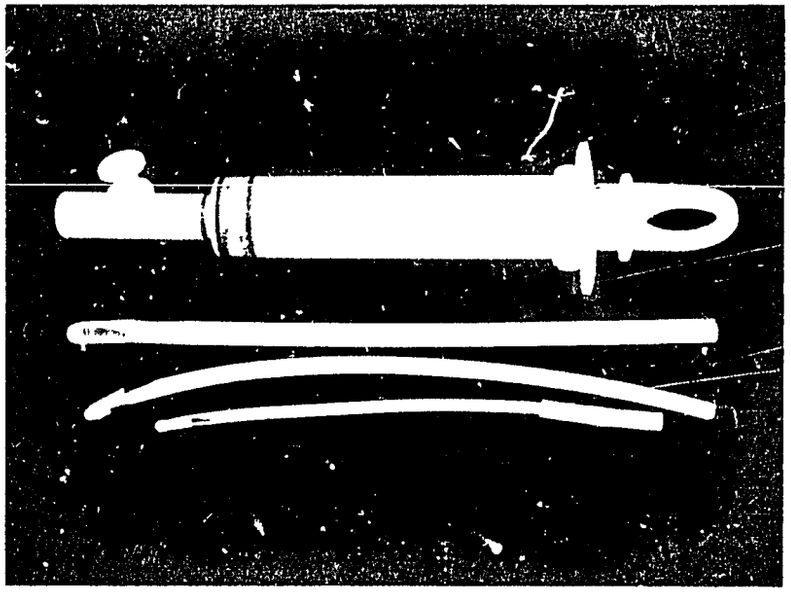


b) Model 300 Syringe Shown with Karman Syringe

FIGURE 1. First Experimental Design of Battelle Syringe



a) Valve closed, handle retracted and locked



b) Valve open, handle fully depressed

FIGURE 2. First Prototype Battelle Syringe

Regulation Conference in Honolulu, and 10,000 of the commercially made syringes shown in Figure 3 were by then available for clinical research contributors attending the meeting. This meeting was held in December, 1973, approximately 6 months after technical redirection of the syringe design problem. Subsequent to this accomplishment, substantial research data have been developed through IFRP studies of this instrument.

Through continuing contact with foreign and domestic suppliers, the syringe design has been picked up by makers in the U.S., Hong Kong, India and Taiwan. It is estimated that at least 150,000 of these instruments have now been made and fielded worldwide.(6)

Responding to an AID directive, a moratorium on further work on the syringe aspirator was imposed in 1974 and persisted until July, 1976. In the interim, some laboratory studies were done on cannulae materials, identifying more durable polyethylenes. This information and details on the original design were provided to a number of U.S. makers and to makers in Hong Kong and India.

As a result of these technology transfer activities, an MR kit was made available by IPAS of Chapel Hill, using some components made in Hong Kong. An Indian product was made available by Chimco Bio-Medical Engineering of Bombay. Continuing review of these instruments was provided by Battelle during their development.

By 1976, deficiencies in the original design had become clear, and these were seen to mainly derive from the plunger assembly used in the commercially made irrigation syringe. The benefit of replacing the snap-fit soft rubber plunger with a rigid piston and replaceable O-ring was first examined by molding a rigid piston and fitting this to the existing plunger. Following proof-of-principle through consultants, IFRP studies in Singapore and field observations, the concept was incorporated in a radical redesign of the syringe handle, ending with the final syringe design illustrated in Figure 4.

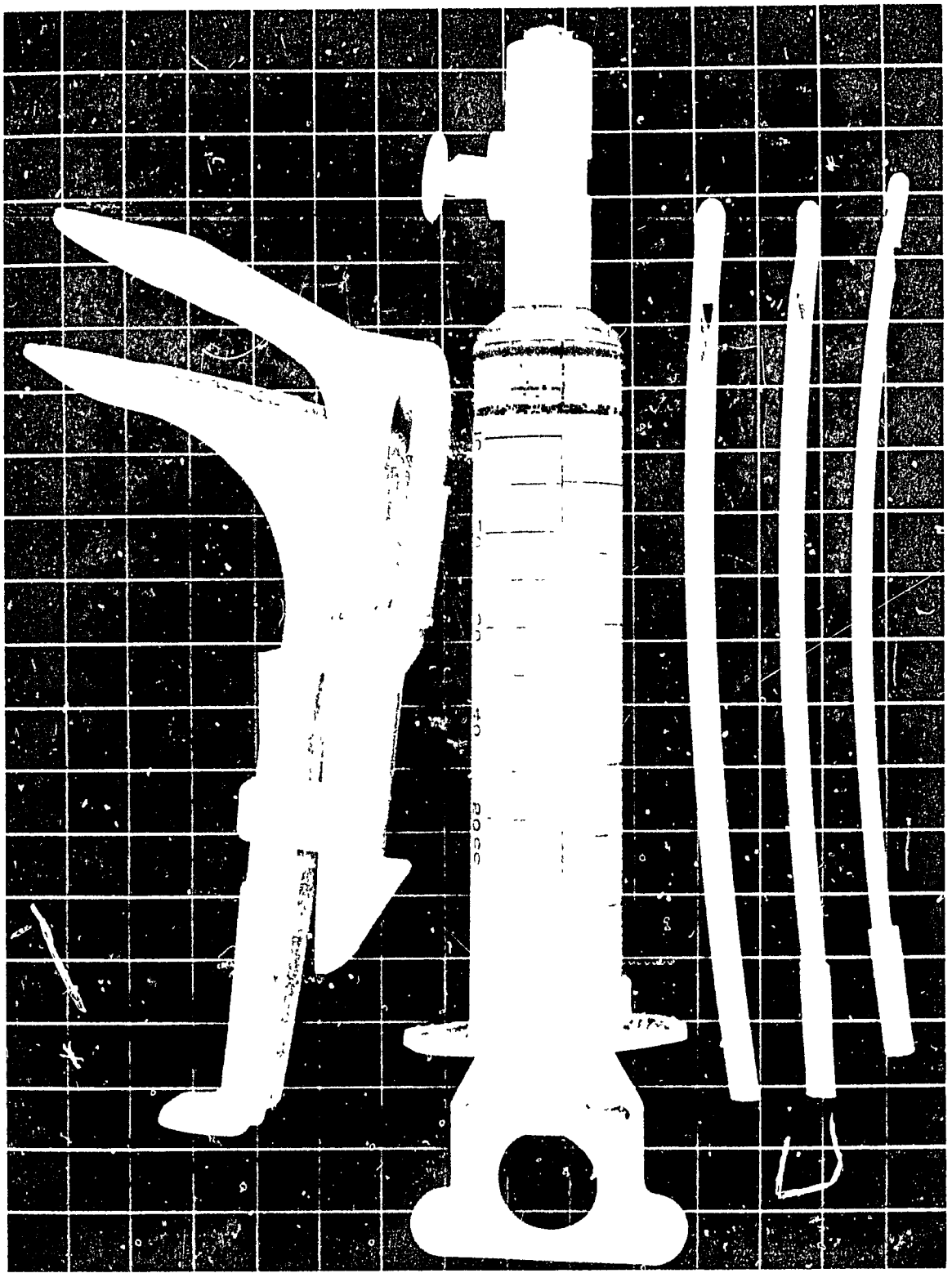


FIGURE 3. First Commercial Version of Battelle Syringe

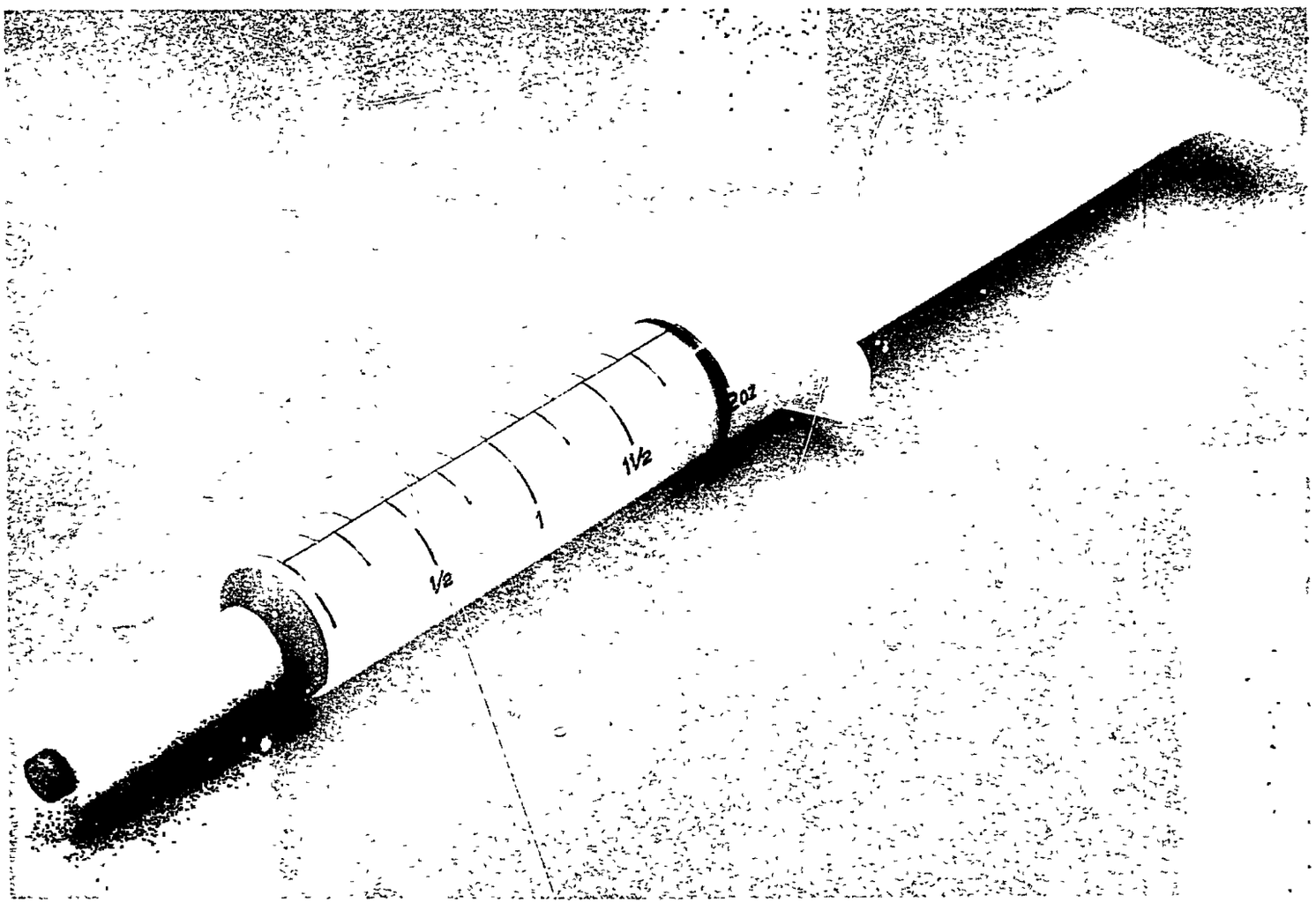


FIGURE 4. Final Version of the MR Syringe

This design has been adopted by IPAS, and preliminary indications are that syringe kit life is extended to several hundred cycles. The amortized cost for instrumentation has accordingly become negligible.

These accomplishments, dating from 1973 with subsequent refinements and improvements indicated above, have permitted private sector donor agencies to take up the task of equipment distribution in Asia, Africa and Latin America. In spite of the withdrawal of AID from direct support of abortion following the Helms Amendment, the affordable instrumentation has permitted the momentum of abortion service proliferation to continue under the auspices of the International Planned Parenthood Federation, the Pathfinder Fund and the Population Crisis Committee, as well as the newer International Projects Assistance Service.

NEGATIVE PRESSURE BOTTLES

The need for this instrument and its place in the armamentarium of vacuum sources has always been unclear. A device that would fit in the category of a hand-held, pre-evacuated container was a part of the original workplan. A first-generation device was patterned after the large syringe developed in 1972, using the same control valve design. This instrument is shown in Figure 5. Work on the instrument was put aside during the burst of activity on the 50cc syringe aspirator.

The idea of a larger, hand-held instrument again surfaced during an equipment session chaired by J.F. Williford at the Menstrual Regulation Conference held in Honolulu in 1973. Discussion centered on the desire for larger container capacity than could be provided by the 50cc syringe, but retaining the vacuum control features of this instrument. Since the desired characteristics could not be met with a syringe design in a straightforward manner, a second look was taken at the negative pressure bottle, applying some new design concepts. Within a month after the Conference, we had evolved an entirely new design and had prepared prototypes.(7) The instrument is shown in Figure 6 in a glass version for automatic evacuation by steam. A second version, in plastic, was developed for evacuation by manual pump, water-powered filter pump or

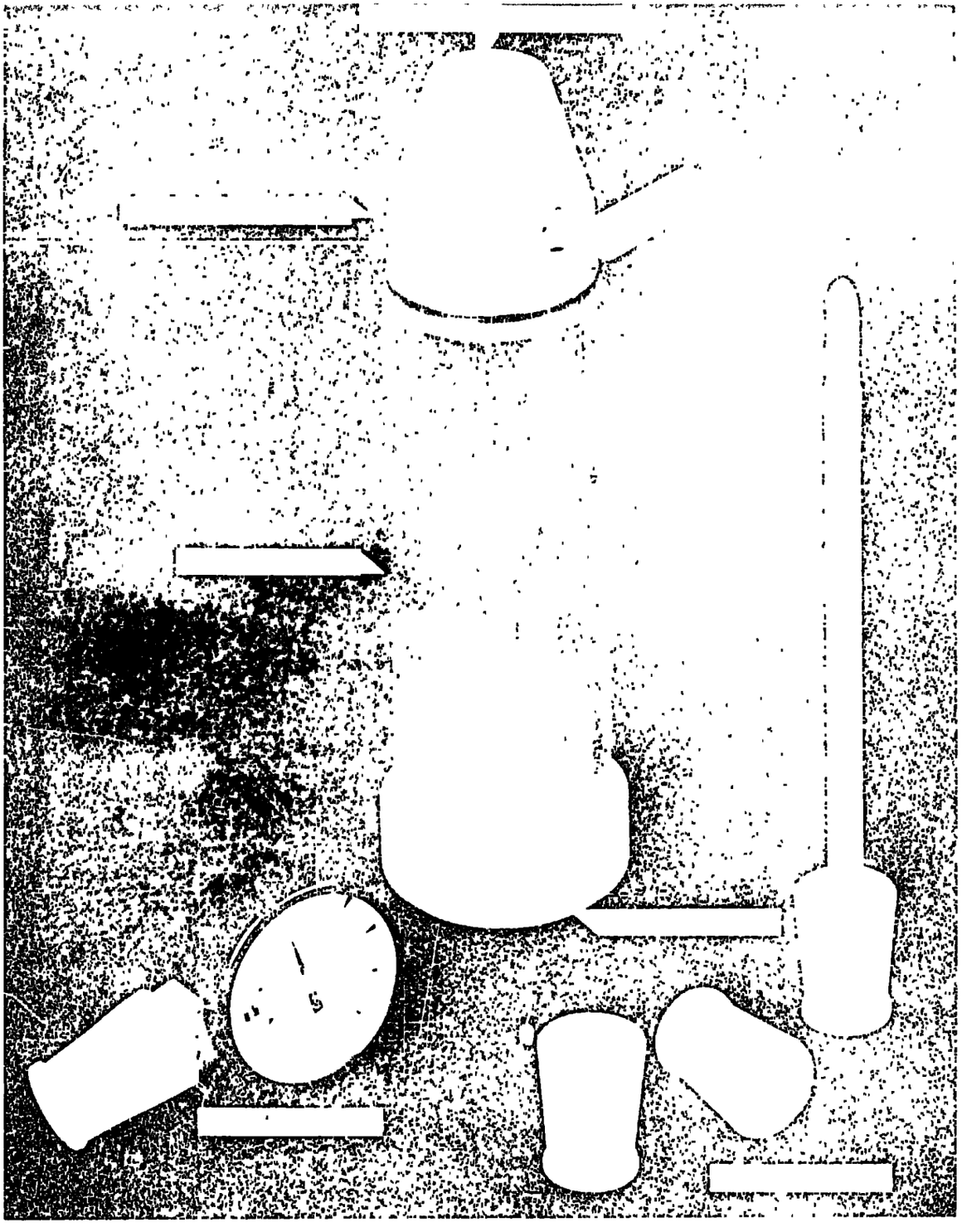


Figure [illegible] Pre-Evacuated Container

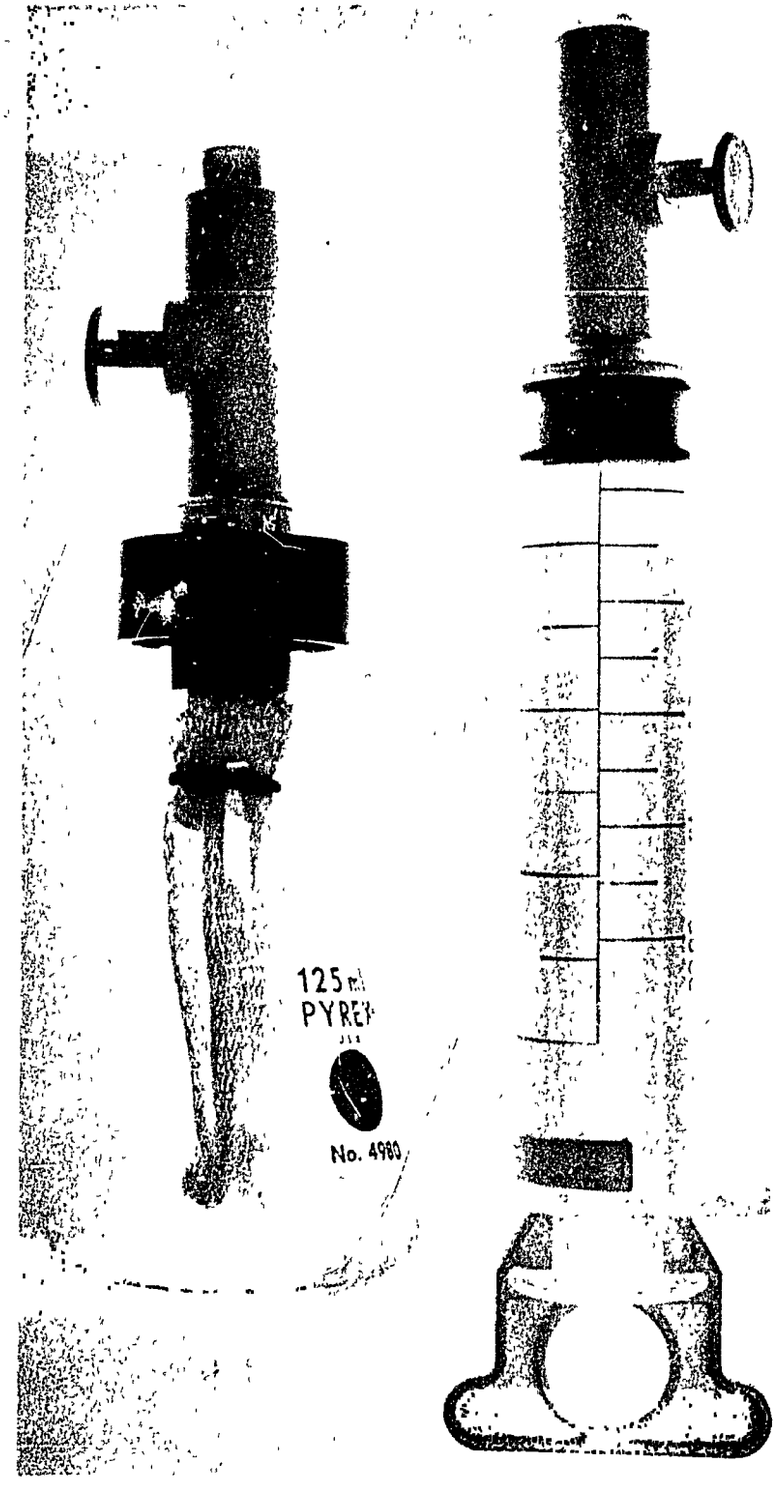


FIGURE 6. Automatic Negative Pressure Bottle. Modified Syringe Shown for Comparison

other means. Supplies of both types were provided for studies by the IFRP, with whom we worked to develop a manual for use and care of both types of instrument.[8]

Although the negative pressure bottles were tested by the IFRP in their first, steam-evacuated version and by our U.S. and foreign consultants in both versions with good results, the design has not been adopted by commercial makers. The design has the virtues of simplicity, economical manufacture and adaptability to larger cannula sizes to exploit larger reservoir capacity. A plot of remaining vacuum as a function of aspirate volume, given as Figure 7, illustrates the potential of the negative pressure bottle approach.

The basic design idea and descriptions of ways to locally improvise negative pressure bottles, using steam evacuation, were presented by J. F. Williford to a Latin American Conference on advances in fertility control.[9]

HAND-POWERED ASPIRATOR

The greater part of our work during the initial contract period was directed toward creation of a nonelectrical system of sufficient capacity to deal with procedures through the first trimester. Our initial effort centered on using existing hardware to the extent possible, as illustrated in the modified tire pumps shown in Figures 8 and 9, and in the foot pump design shown in Figure 10, which uses commercially made pneumatic cylinders.

Whole systems were assembled to examine the key parameters of control valve location, capacity, pumping rate and ultimate vacuum. One of these, assessed by Dr. David in Allahabad, is shown in Figure 11. It used a modified bicycle pump as a vacuum source, commercially available pipe fittings and control valve, and an unbreakable polymethylpentene bottle. A great deal was learned with systems such as these.

Primarily through field visits, we identified clinical problems with such instruments, in part centered on the manipulative difficulties or leakage of any obtainable commercially made control valves and in part

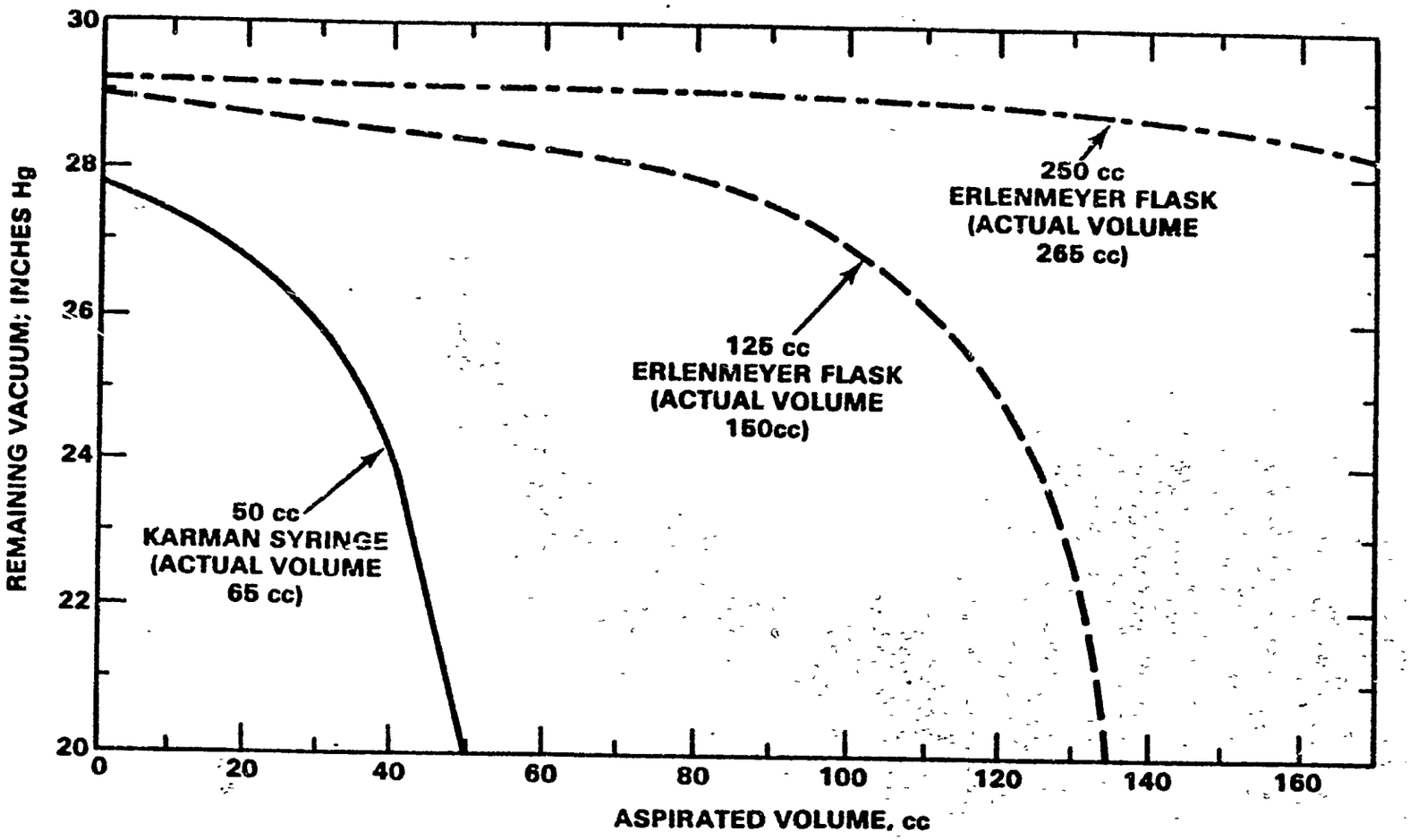


FIGURE 7. Plot of Vacuum Versus Aspirate Volume

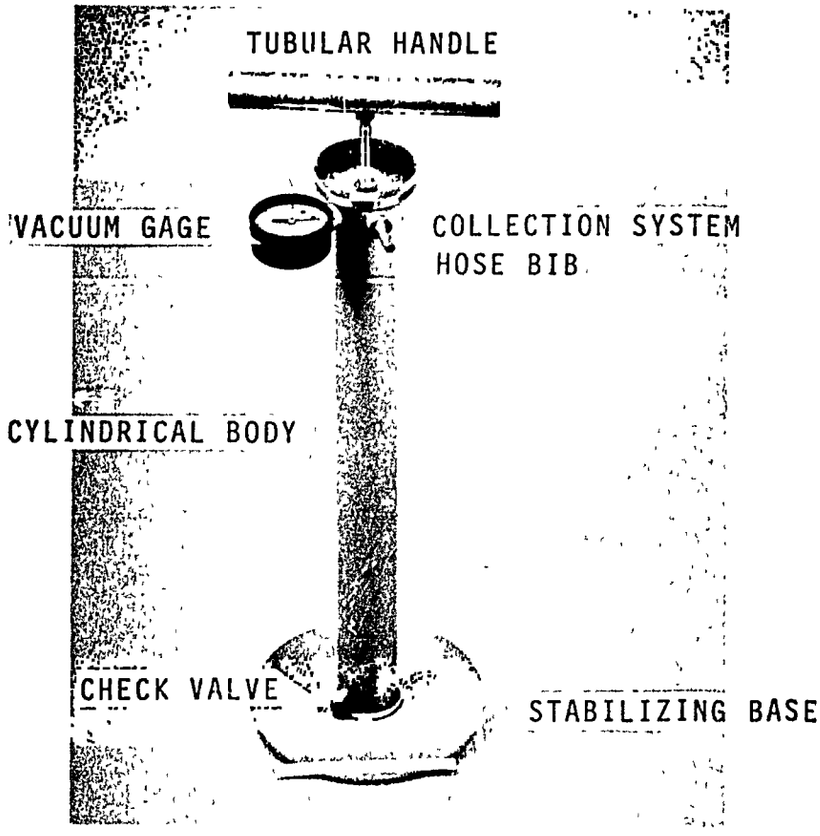


FIGURE 8. Battelle Stirrup Pump

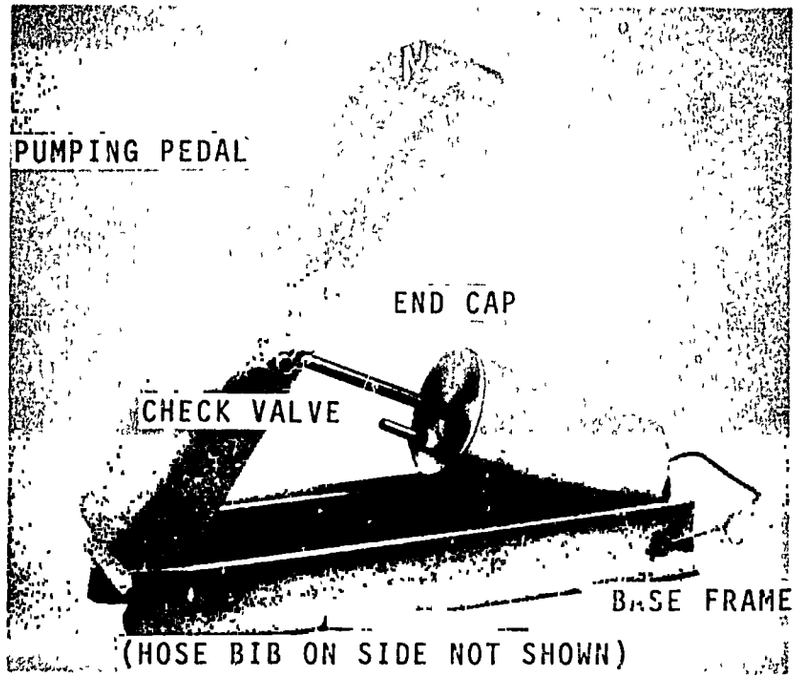


FIGURE 9. Modified Foot Pump

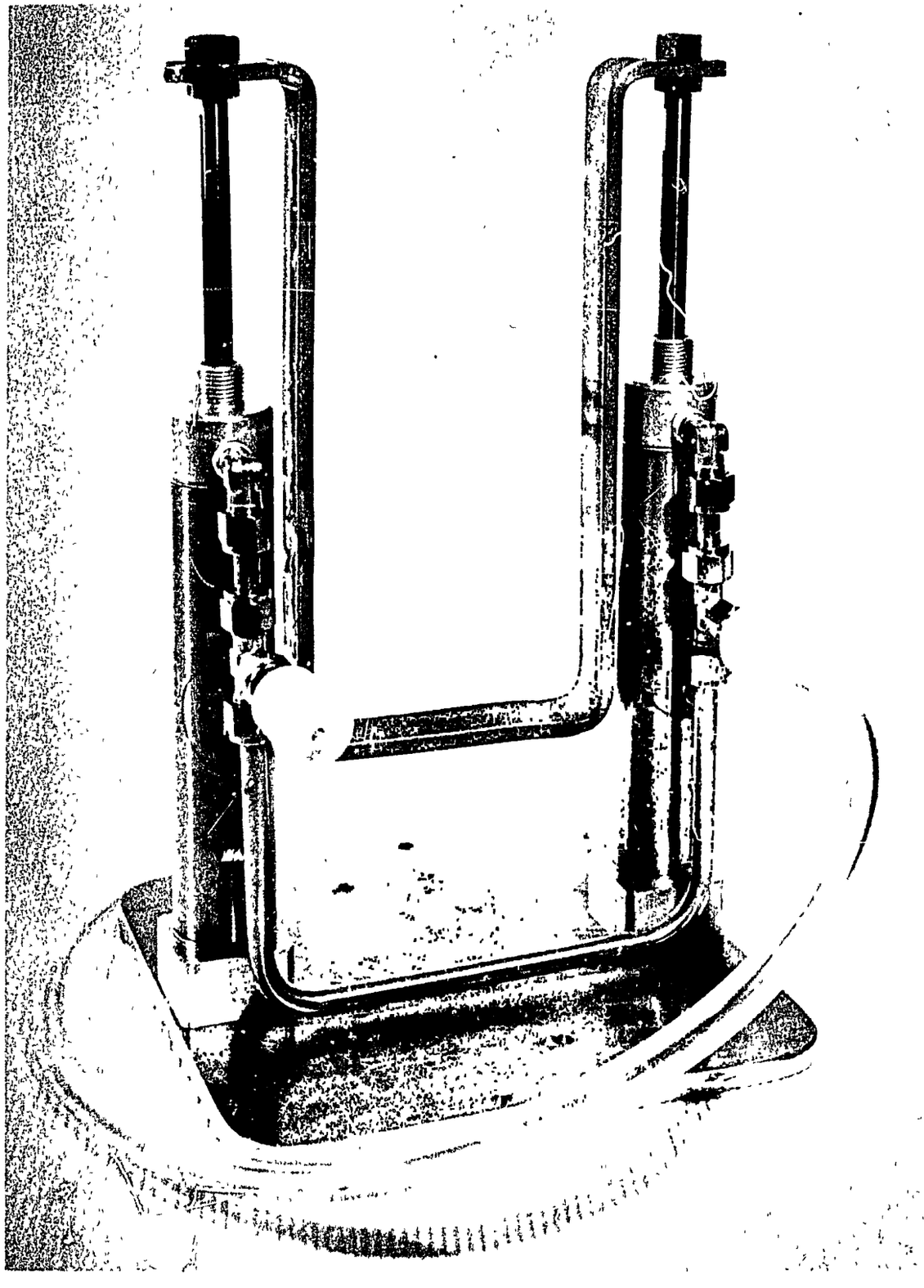


FIGURE 10. Foot Pump Prototype

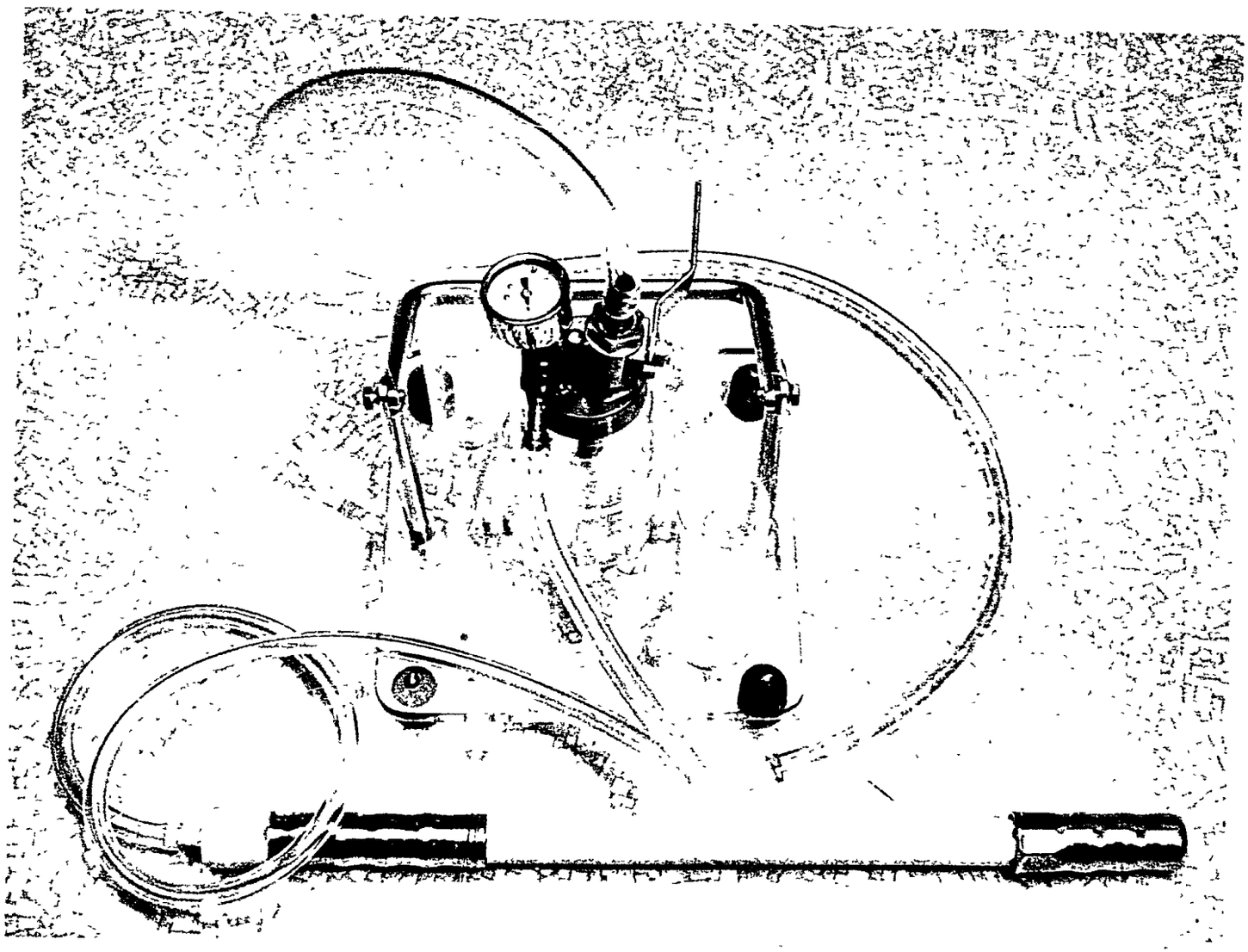


FIGURE 11. Modified Bicycle Pump System

centered on the inability to care for any of the pump designs or to assure that they were not inadvertently modified to become pressure rather than vacuum pumps.

With these findings and observations in hand, we decided that it was necessary to design a completely novel instrument to simultaneously solve the clinical and care problems. The resultant system from this work is shown in Figure 12. The pump design is a radical departure from any prior instruments, and has a number of features adapting it to clinical needs. First of all, the pump works on the downward stroke, exploiting the operator's weight to reduce the amount of work to operate it. The key component in controlling leakage is a simple rubber band check valve which can be cut from a surgical glove thumb, simplifying field replacement. The valve is so effective in holding vacuum that the system will sit for several hours without perceptible vacuum loss. This removes the necessity for an additional valve between the pump and the collection container. The check valve arrangement is shown in more detail in Figure 13. Because of basic design, the pump is very efficient, since dead space is completely eliminated in each stroke and the check valve operates with very little differential pressure. The entire system can be evacuated to provide a vacuum reservoir of 700cc at 27 to 28 inches Hg in less than 25 strokes, accomplished in as many seconds. Another benefit of a pump designed solely for vacuum is that it is not possible to inadvertently modify it so that it operates as a pressure pump. This is an intrinsic feature, and no added safety valves are needed. This basic design has been reported in several publications.[10,11,12,13]

Prototypes of this system were taken to India in September, 1973, in conjunction with an IFRP center tour. Units were left with IFRP contributors in Allahabad, Calcutta and Madras. J. F. Williford accompanied the equipment and identified a number of needed revisions, based on clinical observations of procedures through 12 weeks. These chiefly consisted of redesigning of more secure locking stoppers for the

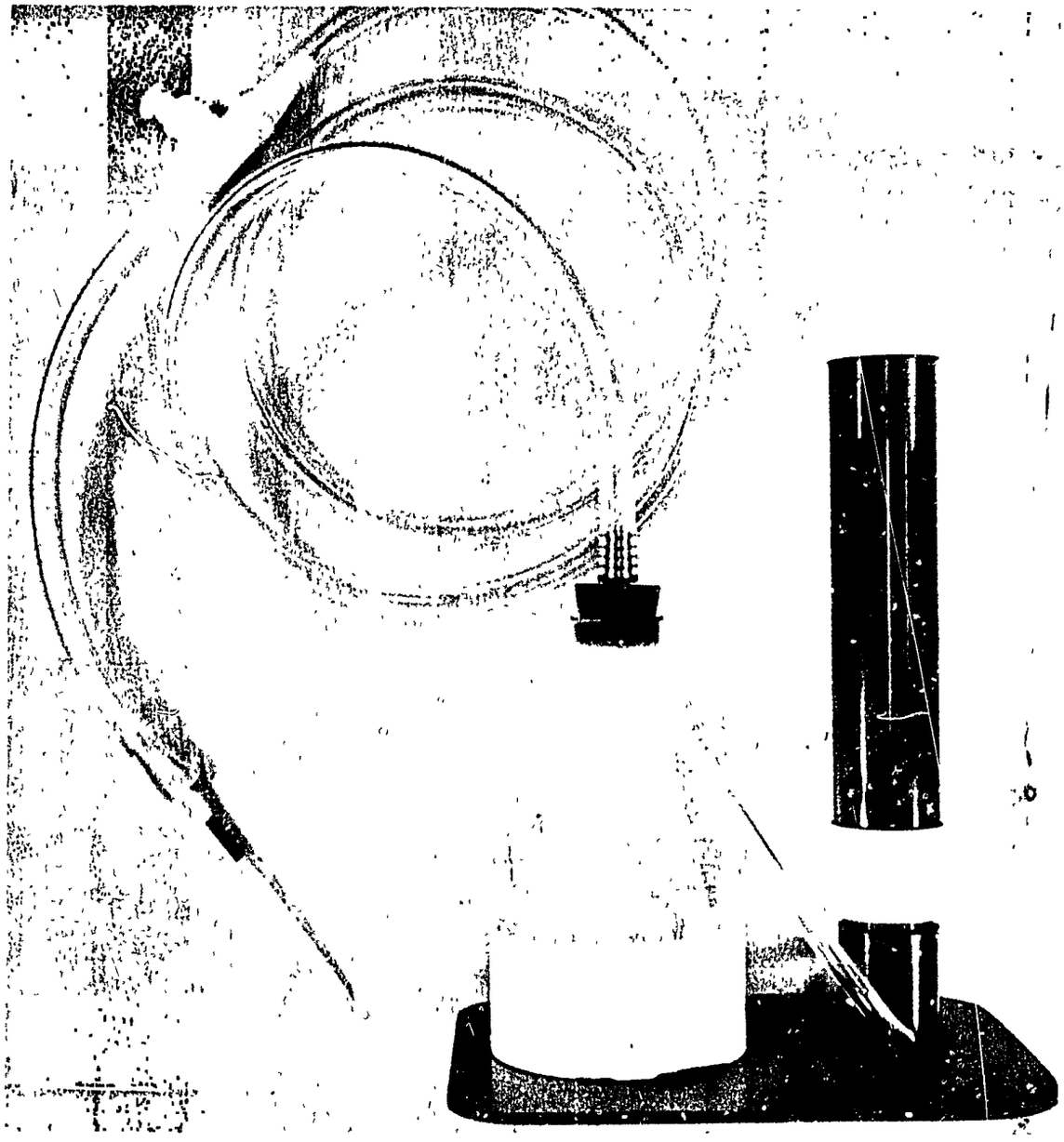


FIGURE 12. Prototype of Battelle Hand-Powered Aspirator, Ultimately Commercialized

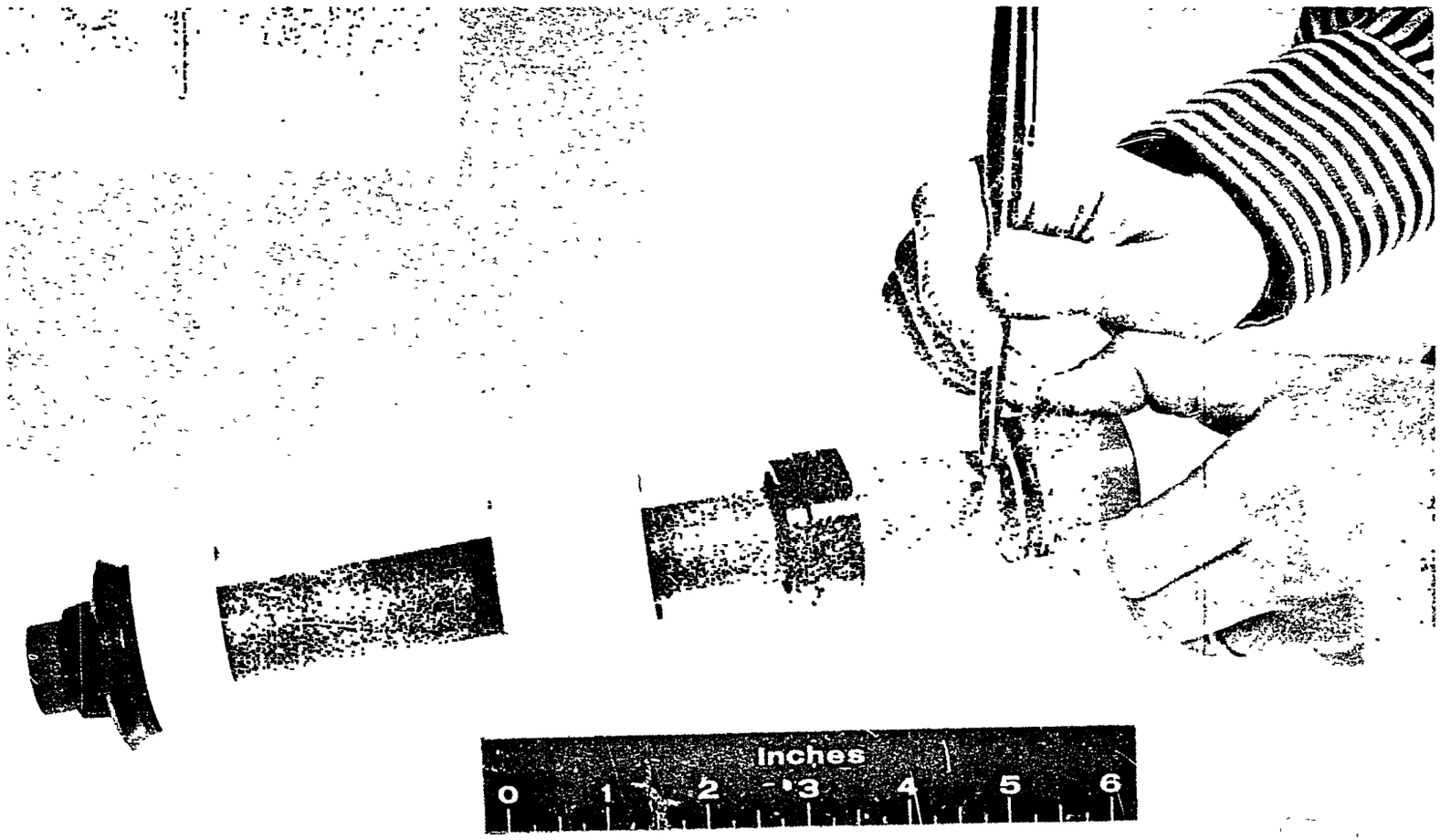


FIGURE 13. Rubber Band Check Valve in Battelle Pump

collection bottle, and moving the control valve to the very distal end of the collection tubing, modifying it to directly accept a range of cannulae.

Units with these modifications were provided to clinical advisors, and the design was accepted for use. Dr. David in Allahabad was particularly helpful in assessing the equipment and providing opportunities to observe field use and care. In the U.S., Dr. Philip Stubblefield used the equipment to perform approximately 150 procedures, throughout the first trimester, without difficulty.

Specifications and detailed designs were subsequently prepared,[14] and a qualified commercial maker was identified. The first 300 kits, procured by AID commodities, were sent to Bangladesh. A subsequent round of kits, incorporating some design refinements, was procured by Battelle for IFRP field studies. This system, with a vacuum cup base for stability, is shown in Figure 14.

In cooperation with the IFRP, an instruction manual and special supplementary questionnaires were developed for evaluating this system.[15,16] Units were placed in a number of IFRP centers, and operation of systems was observed by J. F. Williford during field trips to Asia. Clinical data were reported by the IFRP to Battelle in 1978, indicating that no clinical compromises were necessary as compared to electrical aspirators, using the design as shown in Figure 14.

Prior to receipt of IFRP statistical data, we were able to identify number of minor but important changes for the system, including a complete redesign of the vacuum control valve, collection bottle and base assembly. Additional tooling was prepared to simplify manufacture and assure uniformity of products. Details were provided to known commercial makers in the U.S. and in India. The design, shown in Figure 5, is the final version resulting from refinements on the 1973 design, and is grounded in every detail on clinical feedback and LDC field observations. This design has been adopted by the IPAS and Vista Products

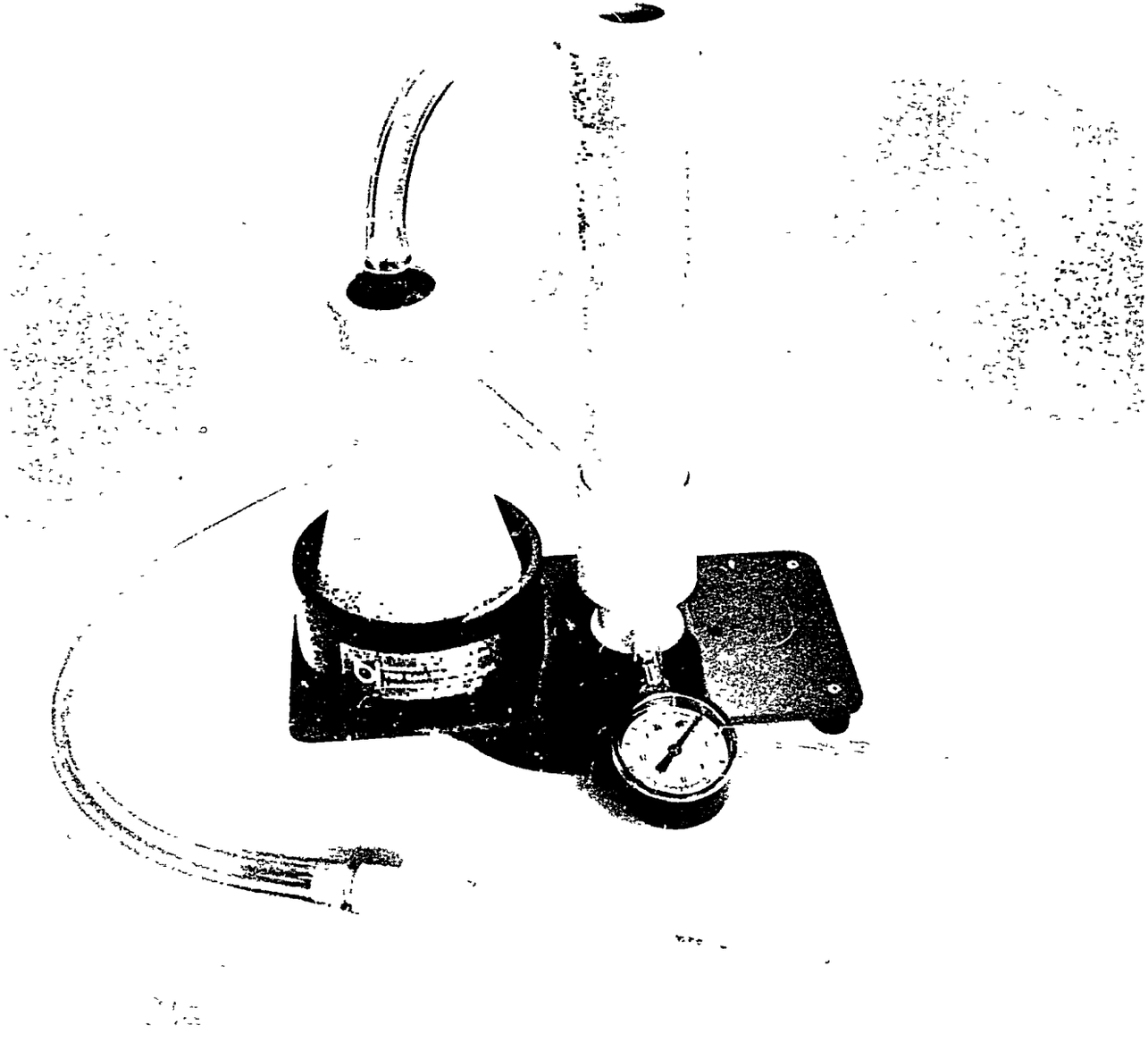


FIGURE 14. Model of Hand Powered Aspirator Supplied for IFRP Studies

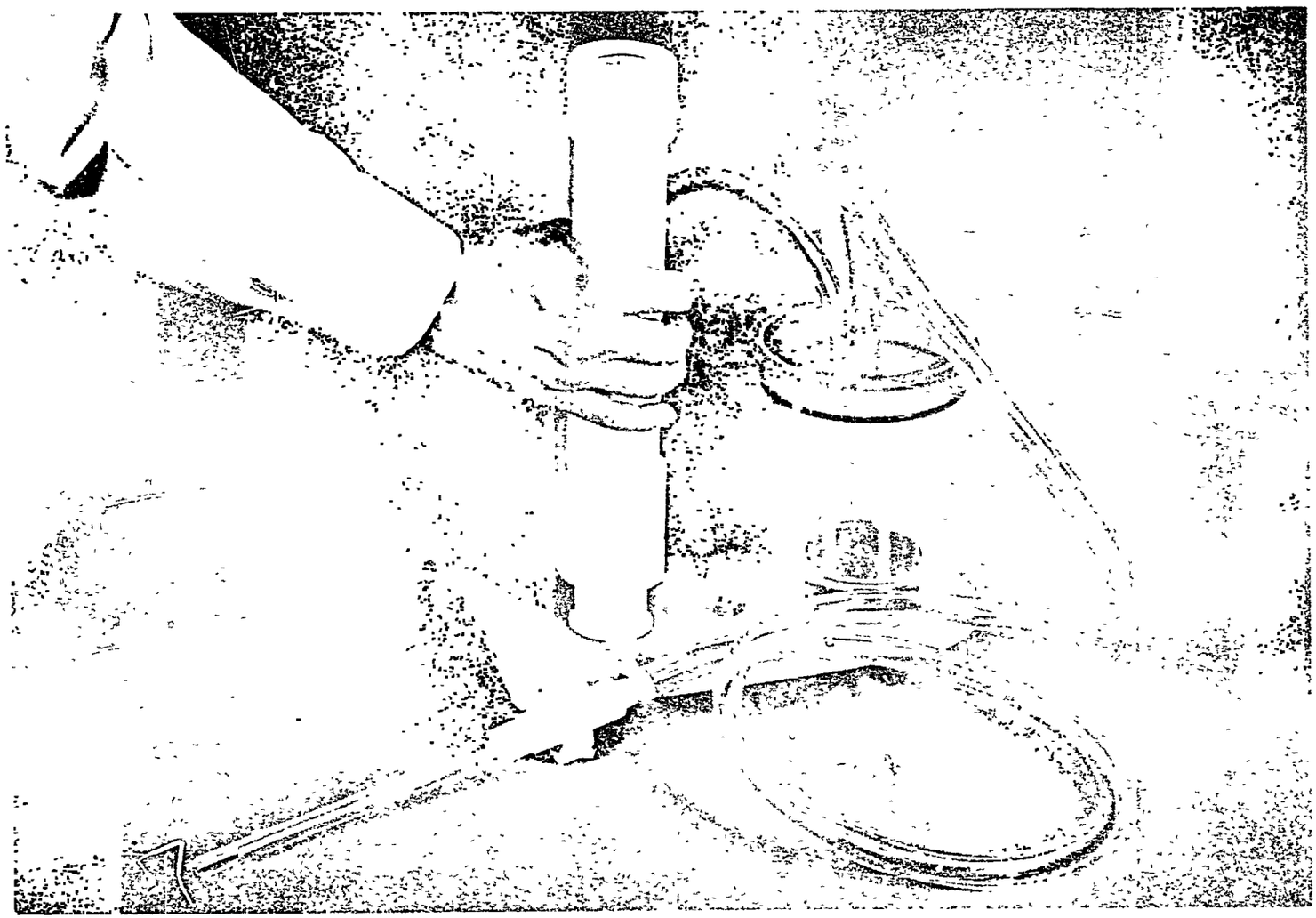


FIGURE 15. Final Design for the Hand Pumped Aspirator

in the U.S., and is being adopted by Chimco Bio-Medical Engineering in Bombay. This version, and the immediately preceding version, are currently being evaluated by the World Health Organization. This instrument and the syringe have been adopted in the Bangladesh family planning program under a training program established by the Pathfinder Fund. A revised instruction manual for the final design system has been prepared.[17]

HISTORICAL REVIEW OF ANCILLARY INSTRUMENTS AND OTHER ACTIVITIES

Although the evolution of new vacuum sources and the introduction of new instruments and methods into LDC's through technology transfer and complementary clinical testing activity by other organizations has been the primary objective of the project, a number of other important activities have been incorporated in the research over the life of the contract. These include:

Cannula materials studies
Comparative cannula pattern studies
Cervical dilation
Tenaculum design
Large cannula system for 2nd trimester D&E
Transfer of sterilization band technology to India

These have been reported in some detail during the course of the project in periodic reports, and are given a summary review in this section.

CANNULA MATERIALS STUDIES

The polyethylene material used by the vendor of the first MR kits procured by AID and distributed at the Menstrual Regulation Conference had low stress crack resistance. Cannulae lasted for only a few uses, and were liable to cracking near the apertures and fracture following repeated cold sterilization. We accordingly obtained samples of polyethylene from a number of primary suppliers and subjected these to stress cracking tests in all major sterilants used in the world. Based on several thousand tests, we identified the best low melt index material for soft cannulae. These findings were provided to all known makers of such cannulae and were adopted by all major suppliers. The durability of cannulae now used internationally has greatly improved as compared to the 1973 product, and instruments are commonly used at least 20 times.

Looking toward substitution of more durable materials for rigid cannulae in sizes from 8mm upwards, we examined a number of candidate polymers by molding test specimens and subjecting these to tests against

sterilants and autoclave conditions. Findings indicated that substitution of newer materials such as polymethylpentene (TPX) for cellulosics and rigid PVC's used in disposable products would yield a durable cannula suitable for repeated use under LDC filled conditions. These findings were shared with major manufacturers of cannulae. One of these, Berkeley Bioengineering, has done a trial run using TPX with favorable results. However, with recent changes in ownership and staff of this company it is unclear at this time whether the product will be made available. IPAS has been interested in making such cannulae, but has been limited so far by available funding for tooling.

COMPARATIVE CANNULA PATTERN STUDIES

Apart from one published study by Andreev,[18] comparative studies of cannulae have been based on clinical indicators. Our theory has been that cannulae patterns as dissimilar as the Karman and Berkeley behave differently in shearing decidual tissues and have differing potentials for damage to underlying myometrium. Although no one else has shared this concern, we were permitted to do one small series in 1976, using histologic principles and newly available image analysis instrumentation.

With Dr. Michael Burnhill's assistance, we were able to examine aspirated materials from pregnancy terminations done with 8mm Karman and Berkeley pattern cannulae. Chorionic villi were hand-sorted out of the specimens under a stereomicroscope, and the remaining washed tissue fragments were then spread in a shallow dish and photographed by transillumination, along with a scale. These photographs were then analyzed with a Quantimet image analysis machine, which displayed data on tissue fragment size distributions in a number of ways. Histology cassettes were packed with tissue fragments, and sections were taken from several locations within the cassette. Following Andreev's lead, we scored numbers of fields in each slide for presence or absence of lamina basalis and myometrium.

The investigator who performed these studies was blinded, and identification as to whether the aspirated tissues were collected with Berkeley or Karman pattern instruments was unknown to him.

Basically, the findings followed our expectations. The Berkeley pattern was found to have a larger average fragment size, rather more lamina basalis, and less myometrial tissue than the Karman. The interpretation from such preliminary data is that the larger opening of the Berkeley leads to a deeper shearing plane than the Karman, lying more nearly at the intersection of the basalis and myometrium. This is evidenced by the larger fragment size and the higher incidence of lamina basalis in the histologic slides. The Karman, as evidenced by the smaller fragment size and comparatively less abundant lamina basalis, shears at a shallower plane and may be thought of as moving downward through the decidua in an incremental, relatively inefficient way. When the larger Karman is moved in and out in a curetting motion, it does occasionally traumatize the denuded myometrium, and the amount of such damage appears to be slightly higher than the Berkeley pattern.

Although we have not yet published these findings, we have discussed them with major suppliers of instruments and with donor organization staff representing The Pathfinder Fund, IPAS, IPPF, the Population Crisis Committee and the World Health Organization. Our findings are supportive of the developing consensus in the U.S. in choice of larger cannula patterns, and we believe that these organizations are now moving in the direction of fielding less traumatic cannulae in larger sizes for international research and service programs.

We will publish this work so that others may expand on the available data and firm up understanding not only of cannula pattern effects, but also vacuum level as related to efficiency of aspiration and likelihood of organ trauma. It is particularly important that this work continue, since clinical studies based on short term symptomatology have been inadequate to resolve questions.[19]

CERVICAL DILATION

Our work on cervical dilation has been based on the general understanding of cervical tissue behavior which has pervaded the field. We

accordingly emphasized mechanical approaches to forcible distension of tissue, selecting approaches which would minimize the chance for perforation or laceration damage. As a main line of approach, we centered efforts on a bivalve mechanical dilator with a number of novel features, and on newer types of force quantitation instrumentation to use in vitro for refinement of design criteria for such a device. A representative dilator design is shown in Figure 16, and a load frame for measuring applied force is shown in Figure 17.

This instrumentation was placed at Johns Hopkins in 1976 for collection of force data. Our intention was to use these data in design of a second-generation instrument which would be spring-driven and lie entirely within the vagina; in short, a mechanical laminaria. For a variety of reasons, we were not able to obtain adequate data from Johns Hopkins for the year or so that the equipment was there.

In discussions with one of our clinical consultants, Dr. Philip G. Stubblefield, we found that Preterm Institute was working on a dilator with some similar features, having four blades. We discussed our findings, based on limited data which had been obtained from Johns Hopkins, and attempted to integrate our efforts with Preterm's by means of a subcontract with them. Although this was never accomplished, we did assist in bringing the Preterm effort to the attention of PARFR, which now supports research on this instrument.

Several things then happened more or less simultaneously. We retrieved the dilators and force measurement instrument from Hopkins so that we could more directly work with excised tissues in collaboration with a nearby consultant. With Dr. Richard Soderstrom's assistance, we were able to both perform and observe force measurements using freshly excised cervices. At the same time, based on our force observations, Preterm strengthened their instrument and reduced the blades to two. Their findings and ours were similar, in that the two-bladed instrument was not an effective dilator. Preterm investigators returned to a four-bladed configuration, greatly strengthened as compared to the original

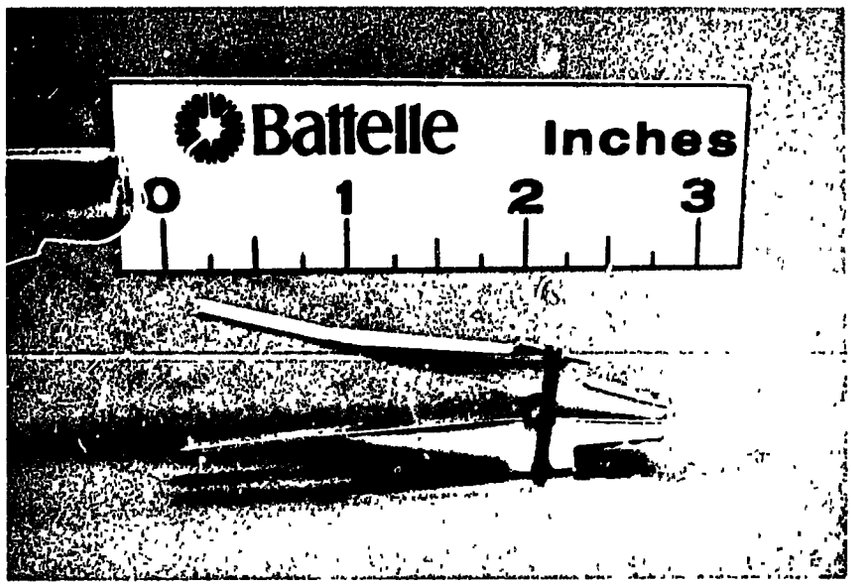


FIGURE 16. Bivalve Mechanical Dilator

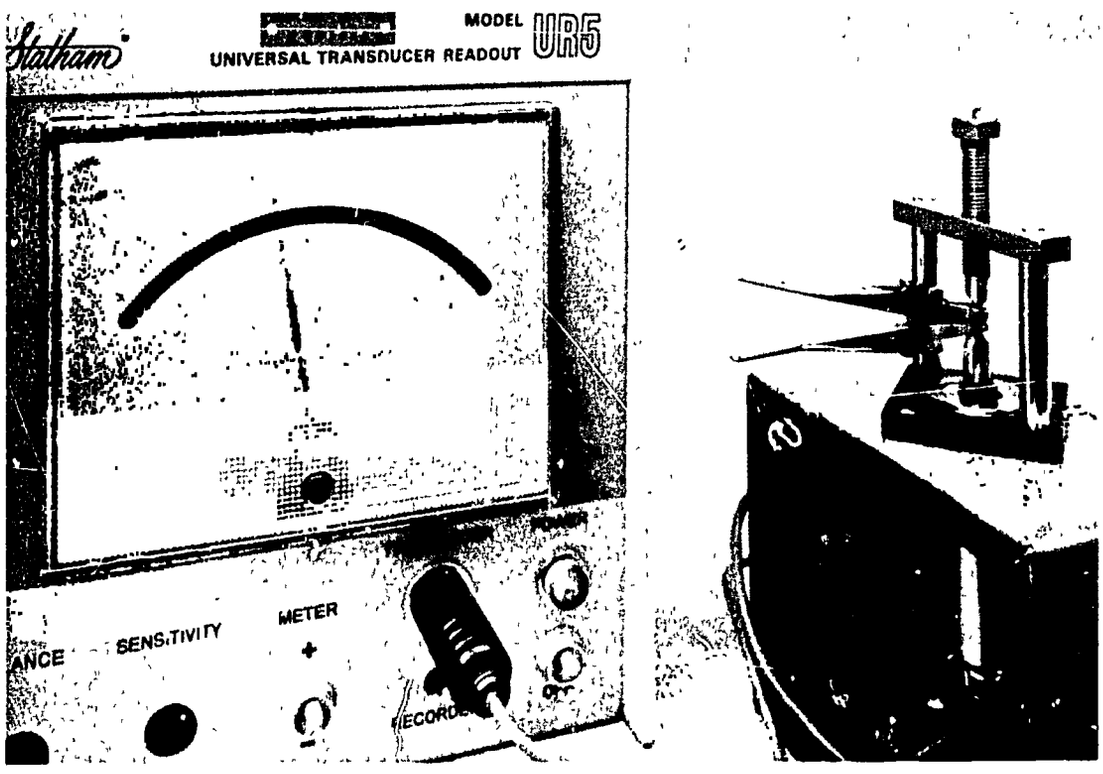


FIGURE 17. Load Frame for Measuring Applied Force

design, based on both our findings. This instrument apparently functions in achieving dilations on the order of 12mm, and results have been reported to Dr. Stubblefield.[20]

Thus, something along the lines we originally suggested appears to be workable, and, in part because of our collaboration, the work continues under PARFR funding provided to Preterm.

However, we see the results of this work as more broadly important through opening of new perspectives and identification of new mechanisms involved in cervical dilation. The unexpected result of using a bivalve dilator is illustrated in Figure 18. Instead of seeing the lateral tissues between the blades stretched in tension, we see rather that tissue flows into the space between the blades. Following up this observation with a reconsideration of what may be happening during cervical dilation, we hypothesized that viscoelastic deformation alone was inadequate to account for the observed behavior, and another mechanism, most likely the movement of fluid, was an inadequately considered and important process during cervical dilation.

An experiment was designed to examine the hypothesis of fluid movement. Essentially, the excised cervix was surrounded by a fitted, split ring which allowed us to compress the tissues. With the ring in place, a 4mm dilator was passed beyond the level of the inner os, and the ring was manually compressed, held briefly, and then pressure was removed and the dilator extracted. The next size dilator was used, and the same procedure was repeated until a dilation of 12mm was reached. Force was unnecessary for passing larger and larger dilators. The exterior dimensions of the organ, restrained by the surrounding ring, were unchanged. Given the achieved dilation and the change in volume, the only reasonable interpretation is that some material has disappeared during the experiment. Interstitial fluid is the most likely candidate material to have moved out of the cervix during the experiment.

These observations and findings were shared at an international conference on the cervix, along with observations we had made on the

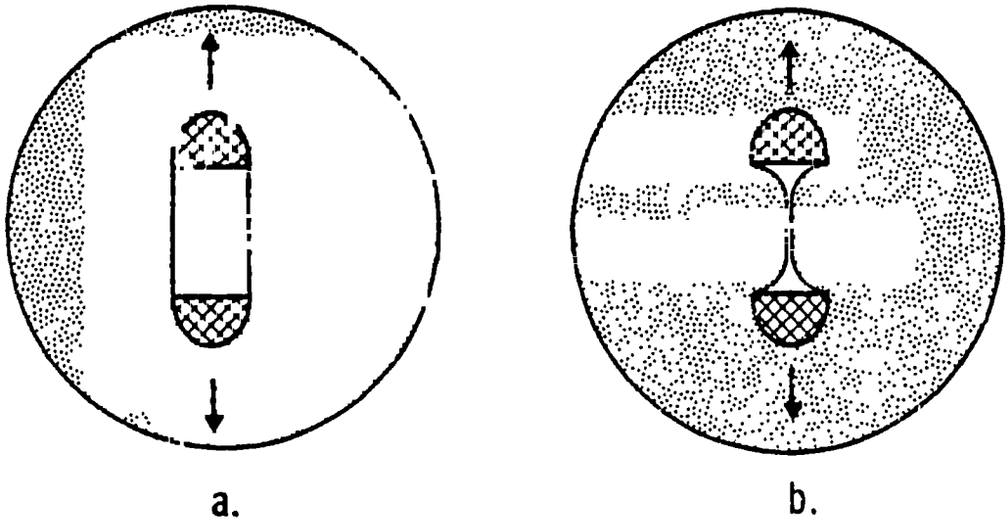


Figure 18. Cross Sectional View Showing Action of Bivalve Dilator; a. as hypothesized. b. as observed.

variation in "stretch modulus" as a function of anatomic site, which we had collected with the assistance of Dr. John T. Conrad at the University of Washington.[21]

Conrad's earlier work on stretch modulus of cervical tissue and the effects of prostaglandins[22,23] may now be seen in a new light, and the action of prostaglandins and other candidate substances may now be reconsidered in light of the probable role of fluid mobility and the role of hormonal balances (notably progesterone) in affecting the amount and mobility of interstitial and intracellular fluid. This insight opens entirely new approaches for future work on dilating the cervix; work which is revelant not only to dilation for therapeutic purposes, but also at term.

Although a number of mechanical approaches, including in situ mechanical laminaria and inside-out approaches to dilation, have been seen as workable, our present feeling is that these approaches have been grounded on an imperfect understanding of the cervix, and are likely to be of limited usefulness. Newer approaches, based on fluid movement and/or extraction can probably be developed soon enough that interim mechanical solutions will have comparatively little impact. However, the mechanical laminaria now under study by Preterm is worth continued support, and, used adjunctively with active substances, may be of continuing value.

TENACULUM DESIGN

In mid-1976 we turned our attention to cervical tenaculae, mainly out of concern that cervical dilation might not yield to newer approaches, and clinicians might be left with the need to apply considerable countertraction to the cervix.

We had discussed design approaches with IPAS, which was adopting an atraumatic design suggested originally by Dr. Karman. Based on these discussions, we decided to procure some of the first IPAS products and evaluate these with the assistance of our consultants and with the IFRP. Increased attention was given to questions of cervical laceration and its management on IFRP forms.

Unfortunately, the new IPAS tenaculae did not completely reflect Karman's original ideas nor our expectations. Our consultants agreed that the instrument had comparatively little merit, and we recommended that the IFRP abandon plans to test it. Using the basic instrument and grinding off the jaws, we made up overlapping jaw designs in a variety of geometries and had these appraised by clinical consultants, including Drs. Stubblefield and Brenner. The most useful configuration, according to Dr. Brenner, is that shown in Figure 19. This instrument is essentially ready for replication by a commercial supplier and clinical evaluation. We have kept IPAS informed on these developments, and expect that they will eventually field the revised instrument.

LARGE CANNULA SYSTEM

We considered a number of approaches to late first and early second trimester uterine aspiration, including the use of vented cannulae which we procured from WISAP, following a commercially available pattern devised by Semm. These instruments were ineffective, both because of the location of the vent tubes (which tended to be obstructed by tissue deformed into the main aperture during use) and the bulk of the tubes, which obstructed the main lumen of the cannulae.

At Dr. Stubblefield's suggestion, and with AID's approval, we added the task of making up a large cannula, handle and collection tubing adaptation for the Berkeley electrical aspirator. This system was used in studies by Dr. Stubblefield in dealing with second trimester abortion from below, using multiple laminaria and vacuum aspiration. The newer arrangement was compared with the Berkeley 12mm cannula, rotary handle and 10mm bore collection tubing. Results indicated that the newer large cannula/handle/tubing arrangement was superior, and results were published.[24] The system used by Stubblefield is shown in Figure 20.

Following a strong expression of interest by the IFRP, based on these favorable results, we prepared tooling for the handle locally and procured blow-molded cannulae from Rocket of London following our design requirements. A corrugated, large-bore collection tubing material was

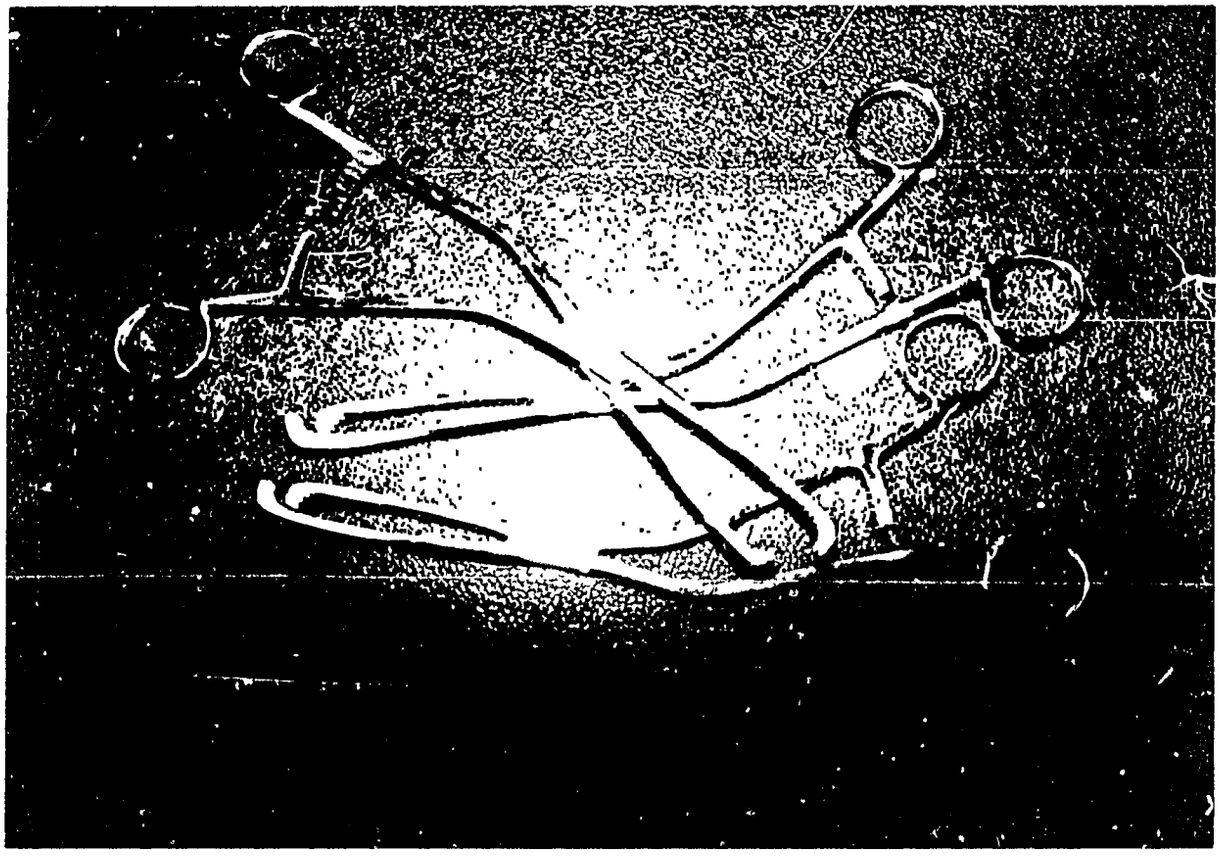


FIGURE 19. Revised Tenaculum Design

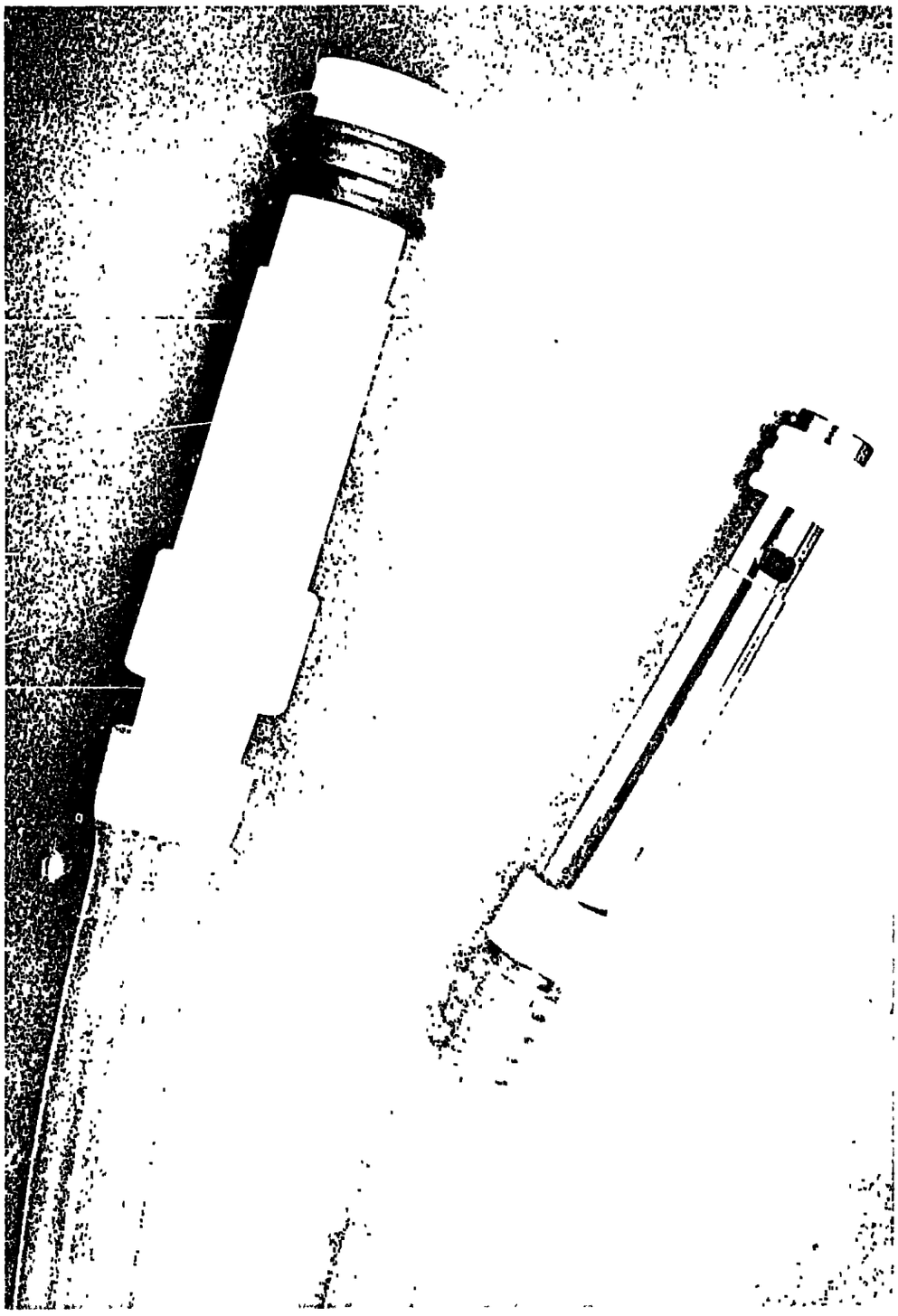


FIGURE 20. Large Rotary Handle Compared to Berkeley Product

found which gave better manipulative control. The effectiveness of all these machine-made components was verified by Dr. Stubblefield, who continues to use the instruments at Harvard Medical School. Sufficient supplies of cannulae, handles and tubing have been supplied to the IFRP to conduct multicenter international studies.

The large cannulae are available from Rocket of London, which owns the tooling. Tooling for the rotary handle rests with a commercial molder who can supply parts for any medical equipment supplier.

TRANSFER OF ELASTIC BAND TECHNOLOGY TO INDIA

Under a technical directive from AID, we identified materials, subjected these to laboratory tests and obtained commercially extruded, unfilled Silastic(R) tubing of the proper size for cutting sterilization bands. Interest in such a product on the part of Chimco Bio-Medical Engineering was already known from field visits in 1976 and arrangements were readily made for them to accept the materials and work out cutting, packaging and sterilization processes with our assistance.

We received early products from Bombay and examined these for dimensional uniformity, cleanness of cutting and response to mechanical tests. We fed information back to Bombay, and subsequently received sterile packaged devices from their first production runs. Based on tests of these and other available rings, the Bombay product appeared to be at least as good (if not better) than other products on our domestic market. We communicated these results to Chimco, and the product was placed on the Indian market. The packaged product is seen in Figure 21.

This accomplishment, although not technically difficult, serves as a good illustration of the timely response which can be obtained when technologists know the people and technical milieu. The total elapse of time for solving materials problems and beginning manufacturing operations in Bombay was only a few months.

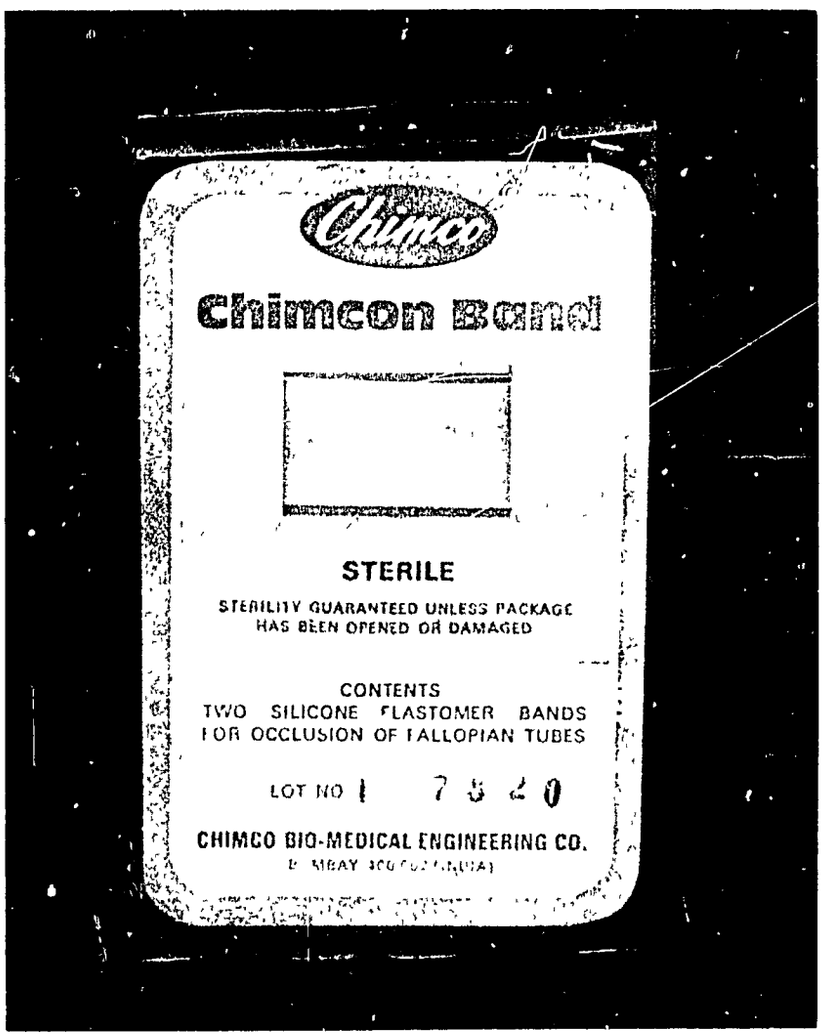


FIGURE 21. Indian-made Band for Female Sterilization

CONCLUSIONS AND RECOMMENDATIONS FOR FUTURE RESEARCH AND DEVELOPMENT

VACUUM EQUIPMENT

Nonelectrical Aspirators

The basic vacuum sources developed under this project appear to meet all of the original criteria of low cost, safety and efficacy and durability in the field. Broad international availability for the MR syringe, which has become ubiquitous in most of Asia and Latin America and parts of Africa, is assured through the activities of a number of makers here and abroad, as well as through the donor roles played by Pathfinder, IPPF, the Population Crisis Committee, IPAS and more recently the World Health Organization.

The hand-pumped aspirator is less far along in terms of international testing and widescale acceptance. However, its future availability appears to be secured through efforts by IPAS and a newly-formed company called Vista Products in the U.S. Donor interest and incorporation into international research and service projects has been provided by The Pathfinder Fund, notably in the new Bangladesh project, and by the World Health Organization, which is just beginning a series of international studies of the instrument.

There are minor points with both instruments which merit some further attention, but these appear to be well within the grasp of present makers.

These developments have resulted in affordable, safe instrumentation to deal with any aspiration procedure up through about 14 weeks LMP without compromise of the patient's safety, as compared to the best electrical equipment available. Favorable economics have permitted private sector organizations to take up the work of providing equipment, thus permitting the continued extension of safe, effective abortion services throughout the world. This activity, which has had a profound and measurable demographic impact, would not have been possible without Battelle's contribution and the effective cooperation between Battelle and the International Fertility Research Program in developing the instruments and validating their clinical efficacy and safety.

Electrical Vacuum Equipment

A number of trends, including the continuing dynamic of urbanization of LDCs through in-migration and the establishment of free-standing clinics, create an increasing demand for affordable and effective electrical vacuum equipment. Most indigenously made vacuum equipment is hard to maintain and operates at marginal effectiveness at best. The extremely durable and effective U.S.-made units are too expensive for most of the donor organizations to afford, and are beyond the means of many LDC clinics.

Our observation is that the Berkeley aspirator has a much greater aspiration capacity and pumping rate than could ever conceivably be needed. The basic design could readily be scaled down (to about 1/4 of present dimensions). This would greatly reduce power requirements, and permit the use of a smaller motor, lighter weight bearings and drive elements. Reduced load bearing capabilities in the pump would permit substitution of molded, engineering plastic components for many parts now made from metal by expensive machining operations. The net results of a redesign and materials substitution centered on scaling down of the Berkeley-type double-ended diaphragm pump would be a smaller, lighter, less expensive unit which would retain the desirable characteristics of the current Berkeley units (i.e., high rate evacuation of collection bottles, high attainable vacuum levels and prolonged service with minimal maintenance.

CANNULAE

A number of things remain to be done to improve the availability of durable cannulae and selection of optimal patterns and vacuum levels.

We have supplied the requisite technology for preparation of durable cannulae for extensive reuse. However, the central problem is an economic one, and U. S. manufacturers whose markets depend on a disposable product have been reluctant to mold cannulae from materials we have identified. Unless one of these companies changes its policy with respect to reusable plastic instruments, the only hope appears to be for an organization such as IPAS to take up the task of meeting the need.

We have performed pioneering studies with tissue fragment size analysis, and have begun the process of correlating these data with histologic results. Advances in understanding that would have been time-consuming and expensive only a few years ago can be readily derived at comparatively little cost using new methods of image analysis. Such instruments are commercially available, and their use is relatively straightforward. We have examined only two patterns of cannulae in one size under one vacuum condition. Findings could be readily extended to a variety of conditions using very few patients (as compared to statistically-based studies grounded on symptomatology during or closely following the procedure). We believe such studies would lead to identification of least traumatic and most efficient patterns for cannulae, and result in optimum levels of vacuum for safest and most effective uterine evacuation for various levels of gestation.

CERVICAL DILATION

Our approaches to mechnical dilation appear to be workable, and may provide some incremental improvements in safety. However, we recommend that the probable role of fluid mobility, identified by Battelle's research, be emphasized in a new round of research studies. These would emphasize comparisons of fluid extraction devices of an inert configuration (similar in some respects to laminaria, but more absorptive and quicker acting) and the use of adjunctive substances to either (a) promote indigenous production of prostaglandin through inflammatory response or (b) directly affect membrane permeability and mobility of interstitial fluid by any of several possible mechanisms.

This new approach holds promise of complete elimination of dangers from mechanical force on insertion or expansion of the dilator or through countertraction by the tenaculum. It is probably possible to avoid expensive and unstable prostaglandins or prostaglandin analogs as bioactive adjuncts to dilation.

CLINICAL STUDIES

It is desirable to broaden the data base on later first trimester abortion using the hand-pumped aspirator, particularly in the latest configuration which has resulted from Battelle's work. Although such studies will be done by WHO, additional work by the IFRP would be valuable.

Studies by others to validate Dr. Stubblefield's findings with the large cannula system developed by us would be useful.

Vacuum aspiration techniques should be examined in comparison with traditional D&C in management of septic or incomplete abortion. Instruments, training and development of an adequate data base for choosing methods are all badly needed in Latin America.

SUMMARY OBSERVATION

We have accomplished the goal of providing affordable, effective and safe instruments for vacuum aspiration. It is hardly surprising that the instruments do not at all resemble those developed by commercial makers for the U.S. market. U.S. demands and the U.S. care infrastructure are so markedly different from the LDC setting that different criteria are necessary for designs and materials. Commercial makers in the West are unaware of these constraints and, for economic reasons, have few motives to develop what is needed.

The accomplishments we have seen in the past few years, and their global impact, would not have been possible without AID support and vision, in conjunction with Battelle's efforts.

We believe that similar kinds of activity could be extended to other fertility control technology needs, notably in the field of female sterilization, with substantial cost/benefit payoffs. The collaborative relationships between Battelle investigators, the International Fertility Research Program and numerous U.S. and LDC clinicians have grown under AID encouragement and nurture into an effective and productive force and means for change.

REFERENCES

1. D.S. Johnson, Termination of Pregnancy: Current Status and Future Directions, Contraception, 5:3, March, 1972.

2. Electrical Vacuum Aspirators, AID Procurement Information Bulletin 73-3, (Reproduced in Progress Report for January-July, 1973).

3. H. Karman and M. Potts, Very Early Abortion Using Syringe as Vacuum Source, The Lancet, May 13, 1972.

4. Medical Advisory Committee meeting minutes, April, 1973 (reproduced in Progress Report for January-July, 1973, pp. 19ff).

5. January-July 1977 Progress Report, pp. 70ff.

6. Personal communications; L.E. Laufe, J. Tomaro, P. Ajmera, 1978.

7. July 1973-January 1974 Progress Report, pp 31ff.

8. Instructional Manual Assembling, Using and Maintaining Negative Pressure Bottles, International Fertility Research Program, October, 1976.

9. J.F. Williford and L.L. King, Equipment Alternatives: History and Prospects; in New Developments in Fertility Regulation, The Pathfinder Fund, 1976.

10. J.F. Williford and R.G. Wheeler, Advances in Nonelectrical Vacuum Equipment for Uterine Aspiration, Advances in Planned Parenthood, Vol. IX, Nos. 3 and 4, 1975.

11. P. Piotrow, Menstrual Regulation Update, Population Reports, Series F-4, 1976.

12. C.S. Dawn, Menstrual Regulation, Dawn Books, Calcutta, 1975.

13. H.R. Holtrop and R.S. Waife, Uterine Aspiration Techniques in Family Planning, The Pathfinder Fund, 1976.

14. R.G. Wheeler letter to J.J. Speidel, September 14, 1973. (Reproduced in July, 1973-January, 1974 Progress Report).

15. Hand-operated Vacuum Pump System, Burnett Instruments; see also IPAS Manual Vacuum System. (Draft material in July-1973-January 1974 Progress Report).

16. Protocol: Evaluation of the Burnett Hand Pump for Vacuum Aspiration, International Fertility Research Program, August, 1976. (Reproduced in January-July 1976 Progress Report).

17. User's Manual for Hand-Pumped Uterine Aspirator (prepared by J.F. Williford and L.O. Foley) printed copies supplied to IPAS, Vista Products and AID Technical Monitor, 1978.

18. D. Andreev, Comparative Histological Investigations on the Evacuated Uterine Mucous Membrane in the Vacuum-Excochleation and Classical Methods of Interruption of Pregnancy, Folia Medica, 1969.

19. M.R. Narvekar et al, A Comparison of Metal and Plastic Cannulae for Vacuum Aspiration, Int J Gynaecol & Obstet 15:433-435, 1978, (and references therein)

20. P.G. Stubblefield and I. Bentov, Alternatives for Cervical Dilatation: Work in Progress, presented at PARFR International Workshop on Pregnancy Termination, Nassau, 1978 (proceedings in press).

21. J.T. Conrad, R.D. Tokarz and J.F. Williford, Anatomic Site and Stretch Modulus in the Human Cervix, International Conference on the Human Cervix, Montreal, 1978 (proceedings in press).

22. J.T. Conrad and K. Ueland, Reduction of the Stretch Modulus of Human Cervical Tissues by Prostaglandin E_2m, Am J Obstet Gynec, 126:218, 1976.

23. J.T. Conrad and K. Ueland, The Stretch Modulus of Human Cervical Tissue in Spontaneous, Oxytocin-induced and PGE_2-Induced Labor, Am J Obstet Gynec, (in press).

24. P.G. Stubblefield et al, A Randomized Study of 12mm and 15.9mm Cannulas in Midtrimester Abortion by Laminaria and Vacuum Curettage, Fertility and Sterility, 29:5, May, 1978.

ACKNOWLEDGEMENTS

We could not have accomplished this project acting independently as technologists. A great many institutions and individuals have provided invaluable insights and, by design, Battelle research has been complemented by clinical studies by others.

The International Fertility Research Program has performed an outstanding service to AID, to the world community at large and to the Battelle researchers through their international studies of the MR syringe and other instruments. In addition to the mass of international statistics and pooled clinical data, the IFRP has provided invaluable help in identifying LDC clinicians to appraise prototypical equipment in advance of systematic statistical studies. Through field observations and discussions with these LDC contributors, Battelle staff have been able to respond to LDC use and care conditions in developing designs, modifying them and selecting crucial materials.

The University of Hawaii, which co-hosted the Menstrual Regulation Conference with Battelle in December, 1973, assisted greatly in the initial introduction of the MR syringe through the IFRP international network of centers.

The Rural Family Planning Project in Allahabad, India, provided invaluable assistance throughout most of the project. Through their kindness, findings on instrument advances were shared at a national conference on rural family planning were presented by J.F. Williford in 1974. Comments provided by Dr. Pramila David and her experience with it had great impact on the final form of the hand-pumped aspirator.

Dr. C.S. Dawn of R.G. Kar Medical College and the India Fertility Research Programme assisted both through his comments on instrument needs and through giving our newer developments visibility in India in his book "Menstrual Regulation," published in 1975.

The Pathfinder Fund has been aggressive in fielding new instruments resulting from our research, and generous in sharing feedback from their

experience. Through their kindness, we were able to present a paper on advances in instrumentation at a conference of Latin Americans held at Airlie in 1976. Their publication of proceedings of this meeting and their work in providing instructional materials for vacuum aspiration has played an important part in timely and informed use of new methods and instruments. The close relationships between Battelle and Pathfinder have made for an unusually timely flow of newly developed information as well as instruments to the field.

Numerous developed country physicians and other experts, whether formal consultants or not, gave continuing support and generously shared their insights. At the risk of offense through omission, these are listed as follows:

Lidija Andolsek
Ljublijana, Yugoslavia

Benjamin Branch
North Shore Clinic

William E. Brenner
University of North Carolina

C. Lalor Burdick
The Lalor Foundation

R.S. Burkman
Johns Hopkins

L. Burnett
Vanderbuilt University

M.S. Burnhill
PIEGO

Julius C. Butler
University of Minnesota

Donn Casey
The Simon Trust

John T. Conrad
University of Washington

George Dennison
Population Dynamics

Merle S. Goldberg
National Women's Health Coalition

H. Robert Holtrop
The Pathfinder Fund

Constance Hussman
PIEGO

Harvey Karman
Los Angeles

Elton Kessel
IFRP

Theodore M. King
Johns Hopkins

Leonard E. Laufe
IFRP

Harry L. Levin
Preterm Institute

Ronald J. Pion
University of Hawaii

Phyllis Piotrow
Population Information Program

Malcolm Potts
IFRP

Richard Soderstrom
The Virginia Mason Hospital

Philip G. Stubblefield
Harvard Medical School

John Thomas
IPAS

Ronald Waife
The Pathfinder Fund

So many physicians, government ministry and industrial people in developing countries have helped us on our field visits that it is impossible to list them all. However, a partial list follows of colleagues from the developing world who merit our special thanks and acknowledgement, with apologies for inadvertent omissions. Additional investigators have contributed through IFRP clinical research projects.

Biran Affandi
Djakarta

Pradip Ajmera
Bombay

Halida H. Akhter
Dacca Model Clinic

Feroza Begum
Dacca Medical College

Hosneara Begum
Sylhet Medical College, Dacca

Sultana Begum
Bangladesh AVS

Rohit V. Bhatt
Baroda

Pouru P. Bhiwandiwala
IFRP

Lessel H. David
Hyderabad

Pramila David
Hyderabad

C.S. Dawn
Calcutta

P.A.C. deSilva
Colombo

Ranajit Dutta
Calcutta

Yu Un Ek
Hong Kong

Atiqur Rahman Khan
Bangladesh Fertility Research Program

S.D. Khandwala
Bombay

T.H. Lean
Singapore

Ajit C. Mehta
Bombay

Shirian P. Mehtaji
Bombay

N.D. Motashaw
Bombay

Biral Mullick
India Fertility Research
Programme

V. Dutt Mullick
New Delhi

D.N. Pai
Bombay

Pandit Patankar
New Delhi

Saroj Pechauri
India Fertility Research
Programme

B.N. Purandare
Bombay

M.I. Ragab
Cairo

Aziaur Rahman
Bangladesh AVS

A. Padma Rao
Manipal

S.S. Ratnam
Singapore

R.P. Soonawala
Bombay

Subita Tejuja
ICMR, New Delhi

Apichart Nirapa Thpongporn
Bangkok