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FETAL GROWTH IN EARLY PREGNANCY

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Key Words

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crown-rump length (CRL)
second trimester of pregnancy

Abstract

Fetal growth (crown-rump length and biparietal diameter) as a function of gestational age was evaluated in pregnancies at 14 to 25 weeks' gestation. The results from this study were compared to those of other investigators who have also reported on the relationships of crown-rump length and biparietal diameter to gestational age. The results from the other studies were found to be similar to those of the present study.

Abbreviations

CRL - crown-rump length
CHL - crown-heel length
BPD - biparietal diameter
LNMP - last normal menstrual period

I. INTRODUCTION

Since the classic study of embryonic and fetal growth by Streeter [13] in 1920, numerous investigators have reported on direct measures of fetal size which correlate with duration of pregnancy, such as crown-rump length (CRL) and less often crown-heel length (CHL), recorded after delivery. More recently, single ultrasonic measurements of the biparietal diameter (BPD) and CRL, and multiple ultrasonic measurements of the skull/thorax area [8] and uterine size components [6,7] have been investigated as in-utero determinations of fetal size at various stages of gestation. The present study was undertaken to assess, based on a large population, the usefulness of CRL and BPD in determining gestational age among a group of patients undergoing elective abortion during the second trimester of pregnancy.

II. METHODS

The present study is based on 4,252 cases of midtrimester abortion by intra-amniotic instillation of hypertonic saline performed at Park East Hospital, New York City, from July 1, 1972 to June 30, 1973. Within 12 hours after the abortion, fetal CRL was measured to the nearest 0.5 cm by the hospital's pathologist. In 476 (11.2%) of the cases, fetal BPDs were determined to the nearest 0.1 cm by the Compound B sonographic scanning technique at the Mount Sinai Ultrasonic Diagnostic Laboratory according to the method described by Donald, MacVicar, and Brown [5]. In the hospital records, gestational age was recorded in completed weeks based on: 1) reported date of the first day of the last

normal menstrual period and 2) physical examination. For the purposes of this study, gestational age was defined as the average of the two estimates when they varied by no more than ± 2 weeks. If the estimates differed by more than 2 weeks, patients were not included in the analysis. This restriction reduced the number of cases for analysis to 220 for BPD and to 2,518 for CRL.

III. RESULTS

Crown-Rump Length. Analysis of the 2,518 pairs of coordinate values of CRL and fetal age indicated a linear relationship in the 14 to 25-week period. The calculated regression of CRL (in cm) on fetal age is:

$$CRL = -3.96 + 1.03 \text{ (gestational age)}; \; R^2 = 0.61$$

For a patient of a given gestional age in the range of 14 to 25 weeks, the expected CRL is given by the above regression equation, and the 90 percent confidence limits on a future CRL are approximated by the expected CRL ± 2.8 cm (Figure 1).

In the 15 to 24-week period, the CRL given by the above regression line is similar to the values obtained by Streeter [13] (Table 1). The largest difference (1.4 cm) between the two estimates was at 15 weeks' gestation, and this difference decreased with increasing fetal age. Although there are differences in the mean CRL values at each gestational age between this and other studies [3,9], all studies have reported similar rates of growth in the CRL (Table II). In this study, the average weekly increase in CRL was 1.03 cm; other studies [2,3,9] have reported values ranging from 1.1 to 1.3 cm per week.

Biparietal Diameter. Based on the 220 pairs of coordinate values for BPD and gestational age for patients at 16 to 25 weeks' gestation, the regression of BPD (in cm) on gestational age is given by:

$$BPD = -0.44 + 0.267 \text{ (gestational age)}; \; R^2 = 0.62$$

The 90 percent confidence limits on a future BPD at a given gestational age are approximated by BPD $\pm$ 0.57 cm (Figure 2). The 50 and 90 percent confidence limits on gestational age for a given BPD are shown in Table III for selected BPD values. These confidence limits show that for a given BPD, gestational age can be estimated within about $\pm$ one week with a confidence of only 50 percent or within $\pm$ two weeks with a confidence of 90 percent. Fifty or ninety percent confidence limits on gestational age for a BPD other than those given in Table III can be derived by linear interpolation of the tabular values. In this study, the average weekly increase in BPD was 0.27 cm and is similar to the BPD growth rates reported by other investigators [1,4,6,11], illustrated by Table IV, which range from 0.26 to 0.32 cm/week.

IV. COMMENT

The reliability of assessing fetal growth by these methods rests upon the accuracy of the determination of both fetal size and gestational age. Using only those cases where the patients' and physicians' estimates of gestational age agreed within $\pm$ two weeks, the results of the present study are comparable to those reported by other investigators [1,4,6,9,11].

The differences in fetal growth parameters reported by different investigators may be due to a number of different factors, including: (1) the methods

of estimating gestational (fetal) age, (2) the status of the fetus at the time of measurement, (3) different methods of determining fetal measurements. Of the above factors, gestational age is probably the most critical in the determination of fetal growth rates. In this study, the analyses included only those patients where gestational ages based on physical examination and onset of the last normal menstrual period (LNMP) were within two weeks of each other in order to exclude cases where gestational period estimates based on reported LNMP were questioned based on the attending obstetrician's assessment of uterine size. Other investigators have used other criteria to determine the reliability of the LNMP estimate of gestational age. Mercer et al. [9] based their estimate of gestational age on three independent estimates. Campbell [4] on the other hand, in the determination of BPD growth, included in his study only those patients who delivered within one week of their expected date.

Some of the discrepancies between the results of different investigations may be attributed to the status of the fetus at the time of measurement. Although the status of the fetus probably does not affect in-utero measurements made by ultrasonography, it may affect other measurements made after pregnancy termination. Streeter [13], for example, based his fetal growth measurements on fetuses that had been preserved in formaldehyde for varying periods of time. Berger et al. [2] and the present study obtained CRL measurements on fetuses aborted with hypertonic saline, and Brenner et al. [3] obtained CRL and CHL measurements on fetuses aborted with prostaglandins.

Of the investigators [3,9] who have reported on the differences between the in-utero measurements of fetal growth parameters and their values after delivery, none have reported large discrepancies. It therefore seems appropriate to

conclude that the variety of ultrasonic methods for determining fetal size are sufficiently accurate.

The prediction equations in this study for both BPD and CRL did not significantly differ when the following factors were also considered: patient's age, race, parity, and service (private, non-private). Sabbagha [12] has also reported no difference in BPD growth rates for women of different races. Although in the latter part of pregnancy (after 34 to 38 weeks) these factors are associated with significant differences in fetal weight [3], previous studies have reported no consistent differences in earlier pregnancy, specifically in the midtrimester.

A method of reliable in-utero determination of fetal growth and assessment of gestation period is of great value to the obstetrician. In high risk pregnancies, particularly those where intrauterine fetal growth retardation is suspected, the timing of obstetrical intervention requires accurate assessments of fetal size. Based on our studies and those of other investigators reviewed here, we believe that ultrasound examination offers a practical and useful measure of fetal growth and prediction of gestational period independent of other clinical estimates.

The 90 percent confidence limits on gestational age for a given BPD are approximately $\pm$ two weeks for gestational ages of 16 to 25 weeks. When both BPD and CRL were evaluated as predictors of gestational age, they did not give a significantly better predictor than BPD alone. Since the BPD measurement is easier to obtain and is of better predictive value compared to CRL, it would appear more advantageous to obtain BPD measurements if only one measurement is to be taken at the time of ultrasonic examination.

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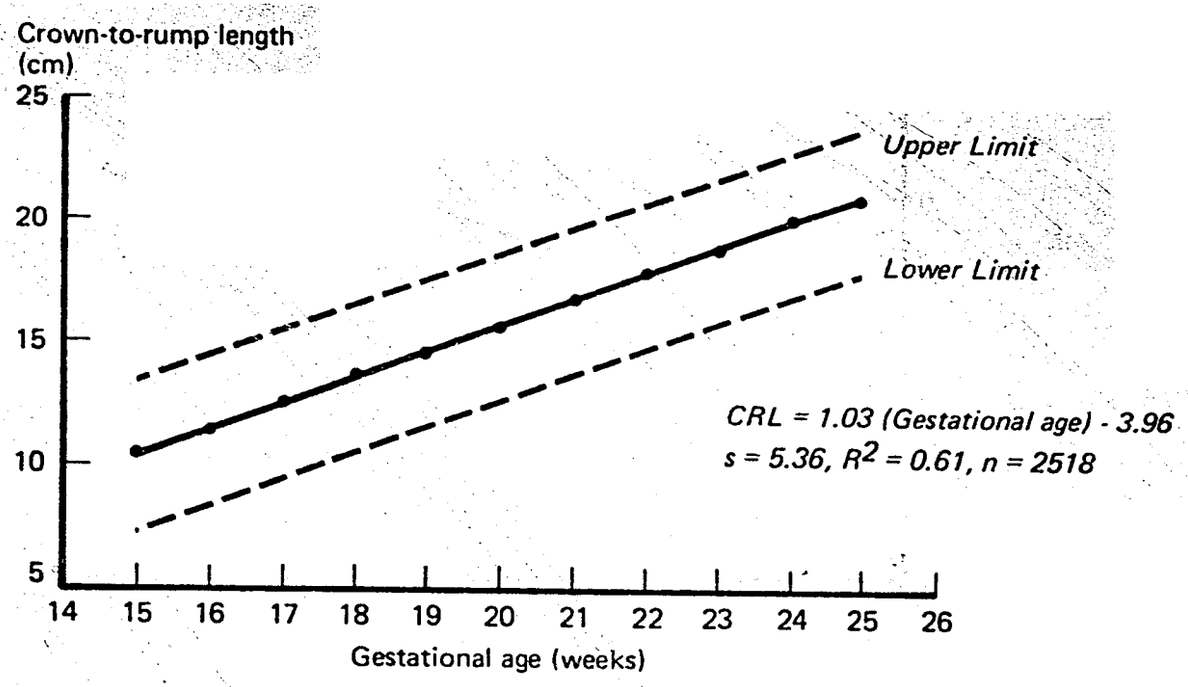

Figure 1. Regression of Crown-Rump Length (CRL) on Gestational Age, and Upper and Lower 90 Percent Confidence Limits on a Future CRL. Each Dot Represents the Mean CRL for a Given Gestational Age. S is the Estimated Standard Deviation About the Regression Line.

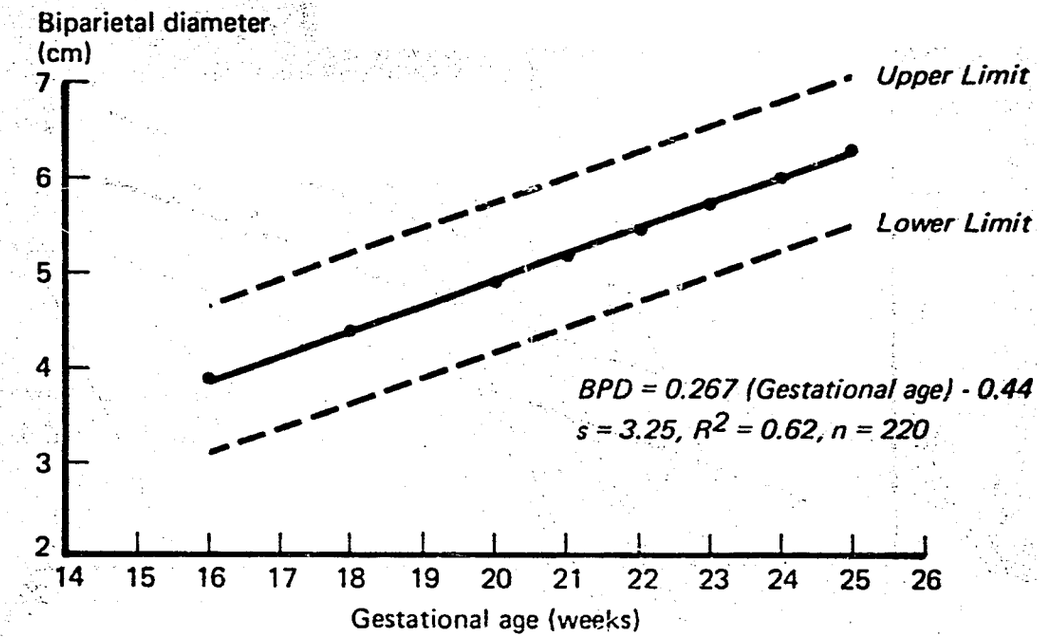

Figure 2. Regression of Biparietal Diameter (BPD) on Gestational Age and Upper and Lower 90 Percent Confidence Limits on a Future BPD. Each Dot Represents the Mean BPD for a Given Gestational Age. S is the Estimated Standard Deviation About the Regression Line.

TABLE I

ESTIMATES OF CROWN-RUMP LENGTH AT DIFFERENT GESTATIONAL AGES FROM STREETER[13] AND THE PRESENT STUDY

Gestational Age (weeks)	Crown-Rump Length (cm)	
	Streeter[13]	Present Study
15	10.1	11.5
16	11.6	12.5
18	14.2	14.6
20	16.4	16.6
22	18.6	18.7
24	20.8	20.8

TABLE II

COMPARISON OF CRL VALUES (in cm) OBTAINED FROM LINEAR REGRESSION EQUATIONS OF BRENNER[3], MERCER[9], AND PRESENT STUDY

Gestational Age (weeks)	Brenner[3] CRL = 1.19(G.A.)*−7.42	Mercer[9] CRL = 1.30(G.A.)*−6.73	Present Study CRL = 1.03(G.A.)*−3.96
14	9.2	11.5	10.5
15	10.4	12.8	11.5
16	11.6	14.1	12.5
17	12.8	15.4	13.6
18	14.0	16.7	14.6
19	15.2	18.0	15.6
20	16.4	19.3	16.6
21	17.6	20.6	17.7
22	18.8	21.9	18.7
23	20.0	23.2	19.7
24	21.1	24.5	20.8

* *Gestational age.*

TABLE III

GESTATIONAL AGE FOR A GIVEN BIPARIETAL DIAMETER – 50 AND 90 PERCENT CONFIDENCE LIMITS

Biparietal Diameter (cm)	Confidence Limits on Gestational Age (weeks)			
	50 Percent		90 Percent	
	Lower Limit	Upper Limit	Lower Limit	Upper Limit
3.0	12.0	13.7	10.6	15.0
3.5	13.9	15.6	12.6	16.8
4.0	15.8	17.5	14.5	18.6
4.5	17.6	19.3	16.4	20.5
5.0	19.5	21.2	18.3	22.4
5.5	21.4	23.1	20.2	24.2
6.0	23.3	24.9	22.1	26.1
6.5	25.1	26.8	23.9	28.0

TABLE IV

COMPARISON OF BPD VALUES (in cm) OBTAINED FROM LINEAR REGRESSION EQUATIONS OF HELLMAN[6], CAMPBELL[4], AND PRESENT STUDY

Gestational Age (weeks)	Hellman[6] BPD = 0.297(G.A.)*−1.649	Campbell[4] BPD = 0.316(G.A.)*−1.26	Present Study BPD = 0.267(G.A.)*−0.44
16	3.10	3.80	3.83
18	3.70	4.43	4.37
20	4.29	5.06	4.90
21	4.59	5.38	5.17
22	4.89	5.69	5.43
23	5.18	6.01	5.70
24	5.48	6.33	5.97
25	5.78	6.64	6.24

* *Gestational age.*

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PT 105

Induction of Abortion with 15(S)-15-Methyl $PGF_{2\alpha}$ (Tham) Vaginal Suppositories

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ABSTRACT

Vengadasalam, D., Lean, T. H. and Edelman, D. A. (Kandang Kerbau Hospital, Singapore, and the International Fertility Research Program, Research Triangle Park, North Carolina, USA). *Introduction of abortion with 15[S]-15-methyl $PGF_{2\alpha}$ [Tham] vaginal suppositories.*

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The repeated administration of vaginal suppositories containing 1 mg 15(S)-15-methyl $PGF_{2\alpha}$ (Tham) successfully induced abortions in 60 of 62 patients. Among patients who successfully aborted, the mean abortion time was 19.0 hours. The mean abortion time was not related to gestational age or parity. Sixty (96.8%) aborted within 48 hours, and 53 (85.5%) aborted within 24 hours. Gastrointestinal side effects occurred for 33.9% of the patients. Diarrhea was the most frequent side effect. The abortion was complete for 40.3% of the patients.

INTRODUCTION

The intraamniotic administration of prostaglandin E_2 (PGE_2) or $F_{2\alpha}$ ($PGF_{2\alpha}$) can successfully induce abortion in patients in their second trimester of pregnancy (2). One drawback to the intraamniotic route is that amniocentesis cannot always be performed prior to 16 weeks' gestation. Although the extraamniotic or intramuscular administration of prostaglandin avoids the technical problems and risks of amniocentesis, some investigators (6, 9) have reported that the extraamniotic administration of prostaglandin is associated with a higher rate of failed abortion before 16 weeks' gestation than later in the second trimester and that the intramuscular administration of prostaglandin requires repeated injections.

Karim and Sharma (7) first demonstrated the feasibility of inducing abortion in patients at 7 to 23 weeks' gestation by the intravaginal administration of suppositories containing PGE_2 or $PGF_{2\alpha}$. Other investigators (1, 3) who have evaluated this procedure have found the vaginal administration of PGE_2 or $PGF_{2\alpha}$ suppositories to be associated with unacceptably high rates of gastrointestinal side effects. The vaginal administration of PGE_2 and $PGF_{2\alpha}$ analogues--15(S)-15 methyl $PGF_{2\alpha}$ methyl ester, 15(S)-15-methyl $PGF_{2\alpha}$ (Tham), and 16,16 dimethyl PGE_2, which have a longer duration of action than their parent compounds—has been reported to be practicable for the termination of first and second trimester pregnancies.

The purpose of this study was to investigate the effectiveness of 15(S)-15-methyl $PGF_{2\alpha}$ (Tham) vaginal suppositories for aborting first and second trimester pregnancies.

MATERIALS AND METHODS

Sixty-two healthy volunteers consented to participate in an evaluation of the abortifacient efficacy of the vaginal administration of suppositories containing 15(S)-15-methyl $PGF_{2\alpha}$ (Tham) (15-me-$PGF_{2\alpha}$).

The patients were from 6 to 20 menstrual weeks' gestation. Most patients (66.1%) were multiparous (mean parity, 1.9) and were from 15 to 43 years old (mean age, 26.6).

The vaginal suppositories, made from a triglyceride base which dissolved at body temperature, contained 1 mg 15-me-$PGF_{2\alpha}$. Initially, 1 suppository was placed intravaginally in the region of the posterior fornix. Two additional suppositories were inserted 3 hours after the first insertion and every 3 hours thereafter until the patient aborted the fetus or until a maximum of 30 mg 15-me-$PGF_{2\alpha}$ (30 suppositories) had been administered. If the patient failed to abort the fetus within 48 hours of the initiation of therapy, the trial was declared a failure. Unless medically indicated, no concomitant therapy was administered until after abortion of the fetus. If the patient aborted the fetus but intervention was necessary to completely remove the placenta, the abortion was termed incomplete.

For all patients, radial pulse, recumbent blood pressure, oral temperature, and respiration were monitored before the initiation of therapy and every 4 hours thereafter until completion of the abortion. Routine laboratory analyses (hemoglobin, white blood cell, differential and platelet counts, and complete urinalysis) were performed before the initiation of therapy, at the time the fetus was aborted, and at 12 hours after the abortion of the fetus.

Patients were not routinely premedicated with

antiemetic and antidiarrheal agents during the early part of the study; later in the study patients were given 2-4 mg Loperimide (Janssen Pharmaceutica, Beerse, Belgium), an antidiarrheal drug, every 8 hours.

RESULTS

The administration of 15-me-$PGF_{2\alpha}$ vaginal suppositories was effective in inducing abortion in patients at 6 to 20 weeks' gestation. Sixty (96.8%) patients aborted within 48 hours, and 53 (85.5%) aborted within 24 hours. Two patients failed to abort within 48 hours. One of these, a 34-year-old gravida 2 at 14 weeks' gestation, was aborted by suction curettage. Cervical dilatation was not necessary since the cervix easily admitted a Hegar #10 dilator at the time of the procedure. The other patient, a 27-year-old gravida 1 at 8 weeks' gestation, was aborted by dilatation and curettage (D&C). For this patient, difficulty in dilating the cervix was encountered. The cervix could not be dilated beyond a Hegar #6 dilator, and the uterus was evacuated with a #1 curette. The inability to achieve adequate dilation suggested a cervical abnormality.

The mean time from the initiation of therapy to abortion of the fetus was 19.0 hours (range, 7.4-43.0 hours) in the 60 successfully aborted patients. The mean abortion times were not significantly different ($p>0.10$) for patients of different gestational ages or for nulliparous and multiparous patients (Table I). The mean time from the initiation of therapy to the onset of vaginal bleeding significantly decreased ($p<0.10$) with increasing gestational age (Table I). However, the time from the onset of vaginal bleeding to abortion was not associated ($p>0.10$) with the abortion time.

No patient had an estimated blood loss of more than 100 ml, and no patient required blood replacement. There were no significant changes in pulse, blood pressure, temperature, or respiration for any of the patients. Compared with patient test results before the initiation of therapy, there were no significant changes in hemoglobin, white blood cell, differential and platelet counts, and urinalysis either immediately after or at 12 hours after 15-me-$PGF_{2\alpha}$ therapy was completed.

Overall, 33.9% of the patients had gastrointestinal side effects. Diarrhea was the most frequent side effect and occurred for 32.3% of the patients. One patient had nausea (2 episodes), and another patient had vomiting (1 episode). The incidence of diarrhea and the mean time to the first episode of diarrhea were not significantly different ($p>0.10$) for patients who were premedicated with Loperimide and those who were not (Table II).

Table I. Mean abortion times

	Number of Patients	Hours from Onset of Therapy to Vaginal Bleeding	Abortion Time (hours)
Gestational Age (completed weeks)			
6-8	37	7.2	18.0
9-12	14	5.5	22.9
13-20	9	4.9	17.0
Parity			
0	20	5.9	18.1
1+	40	6.7	19.5

Table II. Effects of Loperimide premedication

	Number of Patients	Percent with Diarrhea	Mean Time (hours) to First Diarrhea Episode
Premedicated	18	22.2	5.3
Not premedicated	44	36.3	3.7
All patients	62	32.3	4.7

The abortion was defined as complete for 40.3% of the patients and incomplete for 54.9% (Table III). The incomplete abortion rate was significantly higher ($p<0.10$) for first trimester procedures (62.7%) than for second trimester procedures (33.3%). The incomplete abortion rates were similar for nulliparas (55.0%) and multiparas (60.0%).

All patients returned for a follow-up examination after the procedure. No complications were reported. All but 1 patient reported vaginal bleeding after the procedure (mean, 2.7 days; range, 1-5 days). No treatment was necessary for any of these patients.

Table III. Rates of incomplete abortion

Type of Abortion	Number of Patients	%
Complete	25	40.3
Incomplete		
Evacuation with sponge forceps	34	54.9
D&C	1	1.6
Failed abortion within 48 hours	2	3.2

COMMENT

The results of the present study are comparable to those reported by Lauersen and Wilson (8), who

evaluated the use of intravaginal suppositories containing 1 mg 15-me-$PGF_{2\alpha}$ (Tham) and concomitant oxytocin infusion (167 mIU/min) after 24 hours if abortion had not yet occurred to induce abortion in 21 of 22 patients at 13 to 18 weeks' gestation. The mean abortion time was 22.7 hours, and 38.0% of the patients experienced gastrointestinal side effects. In the present study, the mean abortion time was 19.0 hours, and 33.9% of the patients experienced gastrointestinal side effects.

Bygdeman et al. (5), using 15-me-$PGF_{2\alpha}$ (Tham) vaginal suppositories, induced abortion in 7 of 10 midtrimester pregnancies. The mean abortion time was 24.5 hours, and 50.0% of the patients reported gastrointestinal side effects. In the same study, 15(S)-15-methyl $PGF_{2\alpha}$ methyl ester vaginal suppositories were also evaluated. Abortion was induced in 22 or the 23 patients (mean abortion time, 17.2 hours). The authors concluded that the methyl ester of 15-me-$PGF_{2\alpha}$ is about twice as potent as the free acid when administered intravaginally and may be more efficiently absorbed from the vagina. Subsequent studies (4, 10-12) have evaluated the use of 15-me-$PGF_{2\alpha}$ methyl ester contained in suppositories or silastic devices. These studies have reported variable rates of side effects and failure to abort, but have consistently reported a lower mean abortion time than the mean abortion time for the 15(S)-15-methyl $PGF_{2\alpha}$ (Tham) suppositories.

The obvious limitation of the dose schedule evaluated in this study is that the repeated administration of suppositories is necessary to effect abortion. This study does, however, confirm the practicality of inducing first or second trimester abortion by the vaginal administration of prostaglandin. Research efforts to develop a device which can release prostaglandin at a controlled rate should eventually provide a method of abortion that eliminates the disadvantages and risks associated with current methods.

ACKNOWLEDGMENT

This study was supported in part by the International Fertility Research Program (AID/csd-2979). The 15(S)-15-methyl prostaglandin $F_{2\alpha}$ (Tham) vaginal suppositories were graciously supplied by Edward M. Southern, MD, of the Upjohn Company, Kalamazoo, Michigan.

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MENSTRUAL REGULATION SERIES
NO. 30
INTERNATIONAL FERTILITY RESEARCH PROGRAM
CONFERENCE PAPER

MENSTRUAL REGULATION AS A TREATMENT OF SECONDARY AMENORRHEA IN CONTRACEPTIVE USERS

By

Mario Medel, MD
David A. Edelman, PhD

Presented at
Annual Meeting
International Family Planning Research Association
Beverly Hills, California
September 29 - October 2, 1976

MENSTRUAL REGULATION AS A TREATMENT OF SECONDARY AMENORRHEA IN CONTRACEPTIVE USERS

by

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This study was supported in part by grants from the International Fertility Research Program (AID/csd-2979).

Abstract

MENSTRUAL REGULATION AS A TREATMENT OF SECONDARY AMENORRHEA IN CONTRACEPTIVE USERS

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D. A. Edelman, PhD

The safety and efficacy of menstrual regulation (MR)--vacuum aspiration of the uterine contents for the treatment of secondary amenorrhea for women who are no more than 14 days past the expected onset of their menstrual periods--were evaluated in a study of 279 procedures. The rate of significant complications (prolonged bleeding, pelvic infection) was 5.7 percent. Vasovagal reaction was reported for 9.7 percent of the patients. The MR failed to terminate pregnancy for 2.3 percent of the patients. The use of a rapid immunologic pregnancy test (Pregnosticon Dri-Dot) did not appear useful for the diagnosis of pregnancy for women at very early gestational ages.

I. INTRODUCTION

Medical and paramedical personnel are frequently faced with the problem of secondary amenorrhea among contraceptive users. For many of these patients for whom there is no known existing pathology, the etiology of the amenorrhea is often pregnancy because even the most effective methods of contraception are associated with failure.

For those women who present themselves within about two weeks of the expected onset of their menstrual periods, pregnancy cannot be ascertained either by history, pelvic examination, or pregnancy tests. Most of the commercially available immunologic pregnancy tests cannot reliably document pregnancy for patients at very early gestational ages[1]. The physician may treat the amenorrhea by performing a menstrual regulation procedure (MR), i.e., vacuum aspiration of the endometrium within 14 days of the expected onset of a missed menstrual period.

This study evaluates the safety and efficacy of the MR procedure for 279 patients treated for secondary amenorrhea due to a suspected contraceptive failure and the reliability of a rapid immunological pregnancy test.

II. METHODS AND MATERIALS

Subjects

From May 1974 to December 1975, 279 women underwent MR as a treatment for secondary amenorrhea.

Most subjects were less than 30 years of age (69.5%) and were married (73.2%), and 39.8 percent reported one or more previous spontaneous or induced abortions. Only 5.7 percent of the patients were nulliparous, and 16.8 percent were of parity five or more. The following methods of contraception were used at the time of the MR: conventionals, 4.6 percent; IUD, 50.5 percent; systemics, 16.2 percent; and sterilization, 28.7 percent. Most of the women who

had sterilization "failures" had undergone sterilization according to an investigational protocol in which three intrauterine instillations of quinacrine hydrochloride were administered at intervals of one or more months[3].

Procedures

The MRs were performed in a standard manner. Before the MR, a history was obtained and a physical examination including a urinary pregnancy test* were performed. With the patient in the dorsal lithotomy position, the vagina was washed with a bacteriocidal agent, and the uterus evacuated using a 4, 5, or 6 mm diameter, flexible plastic cannula and a 50 cc hand syringe. The aspirate was immediately fixed in Bonin's solution and sent for histological examination. No additional procedures were performed unless the physician believed the evacuation to be incomplete, in which case a sharp curette was used to remove any retained tissue. Most procedures (93.2%) were performed without the use of analgesics or anesthetics, 6.4 percent with only analgesics, and 0.4 percent with paracervical block anesthesia. For 82.3 percent of the patients no mechanical dilatation of the cervix was necessary. Removal of retained tissue with a sharp curette was performed in 0.4 percent of the patients. After completion of the MR, 67.4 percent of the patients had an IUD inserted, 9.8 percent received systemic contraceptives, 2.2 percent conventional contraceptives, and 19.8 percent underwent a sterilization procedure.

All patients were sent home after the procedure and requested to return for a history, physical examination, and pregnancy test two to four weeks after the MR. Follow-up data were obtained for all but one patient.

Definitions and Criteria

At the time of the MR, all patients reported the onset of their menstrual periods was delayed by no more than 14 days. The duration of amenorrhea ranged from 35 to 54 days.

Pregnancy was histologically documented by the presence of products of conception (chorionic villi or membranes) in the uterine aspirate. A presumptive diagnosis of pregnancy was made by the pathologist if no products of

---

*Pregnosticon Dri-Dot, Organon, Inc., West Orange, N.J.

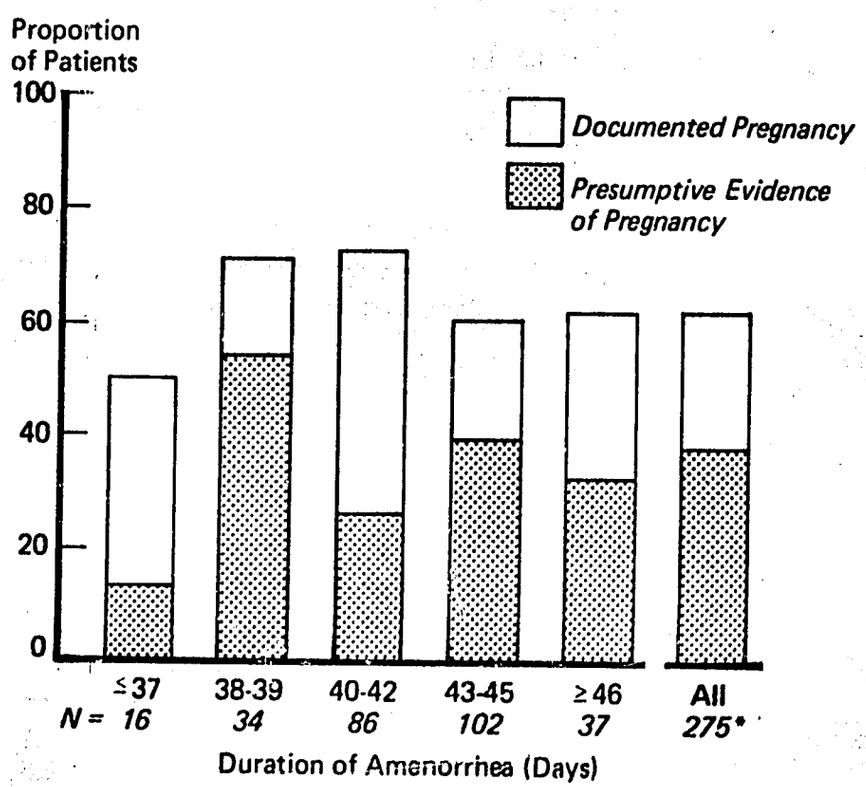
conception were seen, but Sturgis, Aries-Stella signs, or decidua reaction were present.

All patients with a positive pregnancy test at the follow-up visit were followed up for further clinical and histological confirmation of pregnancy.

III. RESULTS

Pregnancy Status

Overall, 25.8 percent of the patients were documented to be pregnant and 35.8 percent had a presumptive diagnosis of pregnancy. The proportion of patients with a presumptive diagnosis of pregnancy was significantly lower ($p<.10$) for patients at less than 38 days of amenorrhea compared to patients at longer durations of amenorrhea (Figure 1). The proportion of patients documented pregnant did not significantly increase ($p>.10$) as the duration of amenorrhea increased (Figure 1).



* *Data missing for four patients.*

Figure 1. Proportion of Patients with Documented Pregnancy or With Presumptive Evidence of Pregnancy by Duration of Amenorrhea.

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Failure of MR

Of the 172 patients who were either documented to be pregnant or who had a presumptive diagnosis of pregnancy, four (2.3%) continued to be pregnant after the procedure. One patient in whom the MR failed to terminate pregnancy had an ectopic pregnancy. For another patient with a bicornuate uterus, the MR had been performed in the nonpregnant side of the uterus.

Eleven patients (3.9%) had positive Pregnosticon tests at the follow-up visit; four of these patients represent MR failures, the other seven do not. These seven patients did not undergo any further treatment, and all of them had negative Pregnosticon tests at a second follow-up visit conducted 15 to 30 days after the first follow-up visit.

Complications

Complication rates are shown in Table I. The most frequently occurring complication was vasovagal reaction which was reported for 9.7 percent of the patients. The incidence of vasovagal reaction was significantly higher ($p<.10$) among patients who had an IUD inserted immediately after the MR (11.2%) compared to patients who did not (6.6%). The rate of clinically significant complications

TABLE I
COMPLICATION RATES

Complication	No.	%
Vasovagal reaction	27	9.7
Cervical laceration	1	0.4
Prolonged bleeding treated by curettage	7	2.5
Prolonged/excessive bleeding not requiring treatment	3	1.1
Pelvic infection		
Fever (>38°C)	6	2.2
Parametritis	3	1.1
Endometritis	2	0.8
Salpingitis	1	0.4
Continued amenorrhea	3	1.1

(prolonged bleeding, pelvic infection) was reported for 5.7 percent of the patients. This rate was not significantly different for patients who were not pregnant compared to all other patients. There was no difference ($p>.10$) in the incidence of pelvic infections among women who were or were not administered prophylactic anitbiotics.

Pregnancy Tests

For amenorrheic patients who were within two weeks of a missed menstrual period, the Pregnosticon Dri-Dot test appeared to be ineffective in discriminating between those who were or who were not pregnant. Of the 197 women who had a negative pregnancy test, only 47.7 percent were documented not to be pregnant based on the histological examination of the uterine aspirate. However, of the 64 women with a positive pregnancy test, only 3.1 percent were documented not to be pregnant (Table II). Of the eleven patients who had positive Pregnosticon tests at the follow-up visit, pregnancy was confirmed in only four (36.4%) of them.

TABLE II
RESULTS OF INITIAL PREGNANCY TEST AND HISTOLOGICAL EXAMINATION OF UTERINE ASPIRATE

Result of Initial Pregnancy Test	Result of Histological Examination*					
	Not Pregnant		Presumptive Evidence of Pregnancy		Pregnant	
	No.	%**	No.	%	No.	%
Negative	94	47.7	80	40.6	23	11.7
Indefinite	6	50.0	4	33.3	2	16.7
Positive	2	3.1	15	23.4	47	73.5

** Data missing for six patients.*
*** Row percentages.*

IV. COMMENT

Vacuum aspiration of the uterine contents appears to be a safe and effective procedure for treating patients with secondary amenorrhea due to a suspected contraceptive failure. The rate of clinically significant complications (prolonged bleeding, pelvic infection) was low--5.7 percent. Vasovagal reaction occurred for 11.2 percent of the patients who had an IUD inserted immediately after the MR compared to 6.6 percent for patients who did not have an IUD inserted. Berger, et al.[2], have also reported a high incidence (7.5%) of vasovagal reactions among patients undergoing IUD insertion. Further studies will be required to verify the increased incidence of vasovagal reactions among patients who have an IUD inserted following an MR procedure. In this study paracervical block anesthetics were used for only one patient. The use of paracervical block may be helpful in protecting the patient against vasovagal reaction following an MR and/or IUD insertion. Comparative studies will be required to evaluate the routine use of paracervical block anesthesia.

Most pregnancy tests, except for the radioreceptor and the radioimmune assay tests for HCG which are not yet commercially available, and knowledge of the patients' contraceptive practice do not appear to be reliable indicators of the patients' pregnancy status. Therefore, performing MR seems to be a safe and recommendable procedure for patients with secondary amenorrhea and for whom there is no known pelvic pathology. The MR procedure is easy to perform, is inexpensive, can be performed on an outpatient basis, and high use-effective contraceptives can be initiated immediately after the procedure. MR is associated with low rates of clinically significant complications. In countries where induced abortion is legally restricted, the MR procedure avoids the high risks of an illegally induced abortion for women with contraceptive failures.

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MENSTRUAL REGULATION SERIES
NO. 32

INTERNATIONAL FERTILITY RESEARCH PROGRAM
CONFERENCE PAPER

THE USE OF TRAINED NURSE-MIDWIVES TO PERFORM MENSTRUAL REGULATION

By

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Presented at
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Beverly Hills, California
September 29 - October 2, 1976

Abstract

THE USE OF TRAINED NURSE-MIDWIVES
TO PERFORM MENSTRUAL REGULATION

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The need to effectively use trained paramedical personnel in the delivery of family planning services is increasingly evident in both developed and developing countries where physicians are faced with an increasing demand for services such as menstrual regulation (termination of a suspected pregnancy within 14 days of a missed menstrual period). Since MR has already been shown to be a relatively simple, safe, and effective outpatient procedure, the Isfahan Health Department in collaboration with the International Fertility Research Program conducted a study to evaluate MR services provided by paramedical personnel at two family planning clinics. The principal topics discussed in this presentation include: (1) identification of social, demographic, and clinical characteristics of the patient groups, (2) evaluation of the safety and effectiveness of 799 MR procedures performed by nurse-midwives, and (3) highlights of the clinical experience, emphasizing the importance of adequate training and experience.

THE USE OF TRAINED NURSE-MIDWIVES TO PERFORM MENSTRUAL REGULATION

By

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This work was supported in part by grants from the International Fertility Research Program, Research Triangle Park, North Carolina (AID/csd-2979).

I. INTRODUCTION*

Menstrual regulation is a procedure for inducing uterine bleeding, usually by vacuum aspiration, within 14 days of delayed onset of menses. As recently as five years ago, menstrual regulation was often done on an inpatient basis and under general anesthesia. The procedure was rapidly simplified. Most procedures are now performed without anesthesia or with paracervical block at the most, and overnight hospitalization is rare. Some clinics, particularly in the United States, are beginning to have nurse-midwives perform the procedures. The advantages are that the procedures are less costly and therefore accessible to a wider range of women, and in addition, the procedure may be more readily acceptable to women in many parts of the world if performed by a woman. It is necessary, however, to establish that menstrual regulation procedures can be performed by qualified paramedical personnel safely, effectively, and efficiently.

This report presents an analysis of 799 menstrual regulation procedures performed at two clinics in Isfahan from June 1974 to April 1976. All procedures were performed on outpatients by certified nurse-midwives. The data were recorded by clinic personnel on standard forms developed by the International Fertility Research Program.

II. PATIENT PROFILE

The mean age of the patients was 28.9 years; three fourths were fairly evenly distributed from 20 to 34 years of age, and only 4.0 percent were less than 20 years of age. Almost 40 percent of the women had no education, and

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*A preliminary report on this study "Menstrual Regulation by Paramedical Personnel in Isfahan, Iran" by Mehdi Loghmani, MD, MPH, and Judith A. Fortney, PhD, was presented by Dr. Loghmani at the Seminar on Population and Family Planning of Iran in May of 1975 at the Center for Population Studies, University of Isfahan, Isfahan, Iran.

only one fourth (25.9%) had completed any education beyond the sixth school year. All except three women (99.6%) were married, 96.2 percent were Muslim, and only 17.1 percent were gainfully employed (Table I).

Fertility History (Table I)

Almost all of the patients (97.7%) were parous and 86.4 percent had given birth at least twice previously. One fourth of the women had had a previous induced abortion. The proportion of all pregnancies recorded as abortions or

TABLE I
SELECTED SOCIO-DEMOGRAPHIC CHARACTERISTICS
OF MENSTRUAL REGULATION PATIENTS
IN ISFAHAN, IRAN, 1974-1976

Characteristics	(N = 799) No.	%	Characteristics	(N = 799) No.	%
Age			Parity		
Less than 20	32	4.0	0	18	2.3
20-24	190	23.8	1	90	11.3
25-29	208	26.0	2-3	265	33.2
30-34	200	25.0	4-5	234	29.3
35-39	120	15.0	6-7	129	16.1
40 or more	49	6.1	8 or more	63	7.9
Mean	28.9		Mean	4.0	
Education (completed years)			Induced Abortions		
0	313	39.2	0	596	74.6
1-3	17	2.1	1	133	16.6
4-6	262	32.8	2 or more	67	8.6
7-9	65	8.1	Unknown	2	0.3
10-12	96	12.0	Spontaneous Abortions		
13 or more	46	5.8	0	748	93.6
Mean	4.9		1	35	4.4
Marital Status			2 or more	14	1.9
Never married	3	0.4	Unknown	2	0.3
Married	796	99.6	Child Loss		
Religion			0	675	84.5
Muslim	769	96.2	1	87	10.9
Other	30	3.8	2 or more	37	4.6
Gainfully Employed			Additional Children Wanted		
Yes	137	17.1	0	582	72.8
No	661	82.7	1	161	20.2
Unknown	1	0.1	2	56	7.0

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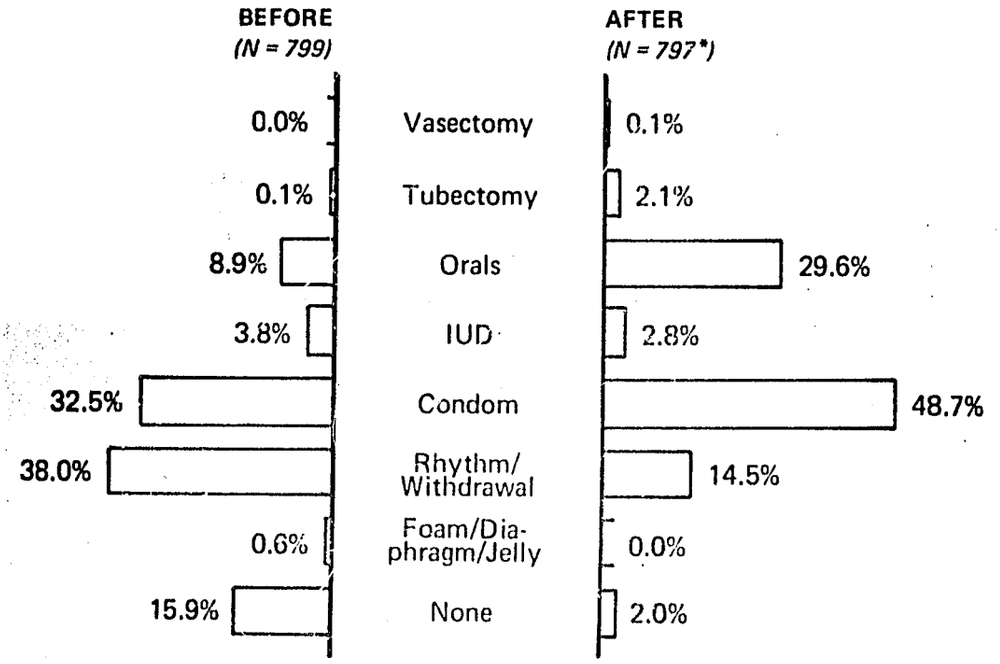
stillbirths (fetal wastage) was 11.5 percent. Child loss was fairly low: 84.5 percent of the women reported that all of their live-born children were still alive. Only 4.7 percent of the women had lost two or more children.

Contraceptive Practice (Figure 1)

Before their menstrual regualtion, 86.9 percent of the women in this study were using no contraceptives (15.9%) or were using a coitus-dependent method such as condom, rhythm, or withdrawal. Of interest, however, were one confirmed tubectomy failure and 101 (13.7%) apparent IUD and oral contraceptive failures. The Isfahan Health Department used the menstrual regulation service as a backup for contraceptive failures; this accounts for the high percentage of IUD and pill failures among these patients.

After the menstrual regulation procedure, almost all of the women (98.0%) indicated that they intended to use contraceptives; 29.6 percent accepted oral contraceptives.



* *One patient lost to follow-up and one patient using Depo-Provera.*

Figure 1. Contraceptive Use or Acceptance in the Month Before the Procedure and at Follow-Up Visits Usually One Month After Menstrual Regulation, Isfahan, Iran, 1974-1976.

A large number of women in this study (582) reported that they wanted no additional children (Table II). Only 16 of these women, however, chose tubectomy to control their fertility after the procedure, while two thirds chose a coitus-dependent method (64.8%) or no method at all (2.6%).

Preexisting Medical Conditions

Almost a tenth (9.8%) of the patients had unspecified preexisting pelvic conditions. Since these and the three preexisting psychiatric conditions did not appear to affect the complication rate, they were not excluded from the study.

III. CLINICAL PROCEDURES

All procedures were performed in a standard manner using flexible plastic Karman cannulae and plastic hand syringes. Prophylactic antibiotics were given to almost all women in this study. Almost two thirds (64.2%) of the procedures were done with no anesthetic or analgesic. Thirty-five percent of the patients (280) received analgesics; only four patients received a paracervical block; and two received general anesthesia.

A procedure was defined as incomplete if a repeat procedure or D&C was required. A procedure was defined as a failure if the patient had a confirmed continuing pregnancy at the follow-up visit, usually one month after the initial procedure.

TABLE II
WOMEN WANTING NO ADDITIONAL CHILDREN BY POST-PROCEDURE METHOD OF FERTILITY CONTROL USED OR ACCEPTED
ISFAHAN, IRAN, 1974-1976

Post-Procedure Contraceptive Method	No.	%
None	15	2.6
Withdrawal/rhythm	94	16.2
Condom	283	48.6
IUD	18	3.1
Orals	153	26.3
Tubectomy	16	2.7
Vasectomy	1	0.2
Depo-Provera inject.	1	0.2
Total	582	**100.0**

IV. COMPLAINTS AND COMPLICATIONS

The menstrual regulation procedure usually has few complications. During the first phase of this study the complication rate was abnormally high due to a problem with the syringe at one clinic and the initial inexperience of the nurse-midwives. Faulty sterilization caused the plunger of the syringe to stick so that it could not be retracted far enough to create an adequate vacuum; thus, the procedure had to be repeated several times causing discomfort to the patient and often resulting in inadequate aspiration and an incomplete procedure.

Because of the equipment difficulties and inexperience of the nurse-midwives, the complication rates in Table III are given for three periods: (1) June to December 1974 (the equipment problem worsened gradually), (2) December 1974 to February 15, 1975 (new equipment was used), and (3) February 16, 1975 to April 1976 (the nurse-midwives received additional training at the beginning of this period).

During the first period, almost 30 percent of all patients (N=142) had at least one complication (a few of which were potentially serious), 10.6 percent (15 patients) had to return to the clinic for a repeat procedure to remove retained tissue, and three patients with positive pregnancy tests at follow-up elected to continue their pregnancies. All of the continued pregnancies and 14 of the 15 repeat procedures occurred at the clinic with the syringe problem.

Replacement of faulty equipment and new sterilization procedures cut the complication rate in half during the second period and virtually eliminated the serious complications.

The increased experience of the nurse-midwives and additional training by a highly skilled obstetrician-gynecologist in mid-February 1975 were also important in reducing complications. For 571 subsequent menstrual regulations performed by the nurse-midwives, there were no failures, only one incomplete procedure, and a complication rate of only 4.0 percent. None of these complications were considered serious, and none occurred during the initial procedure.

TABLE III
IMMEDIATE AND DELAYED COMPLICATIONS ASSOCIATED WITH MENSTRUAL REGULATION PROCEDURES DURING THREE TIME PERIODS ISFAHAN, IRAN, 1974-1976

Complications	June 1974-Nov 1974 (N = 142)*		Dec 1974-Feb 15, 1975 (N = 86)		Feb 16, 1975-Apr 1976 (N = 571)	
	No.	%	No.	%	No.	%
Immediate						
Blood loss more than 100 ml	20	14.1	1	1.1	0	0.0
Shock	1	0.7	0	0.0	0	0.0
Vomiting**	17	12.0	0	0.0	0	0.0
Fever more than 38°	18	12.7	0	0.0	0	0.0
Women with one or more immediate complications	32	22.5	1	1.1	0	0.0
Delayed						
Bleeding requiring curettage	7	5.0	0	0.0	2	0.4
Bleeding not requiring curettage	1	0.7	7	8.1	8	1.4
Fever requiring antibiotics	5	3.5	0	0.0	11	1.9
Other***	3	2.1	5	5.8	3	0.5
Women with one or more delayed complications	15	10.6	12	14.0	23	4.0
Total number of women with one or more complications	42	29.6	13	15.1	23	4.0
Repeat procedure required at follow-up visit	15	10.6	2	2.3	1	0.2
Pregnancy continued	3	2.1	0	0.0	0	0.0

** N = 141 for delayed complications in this group.*
*** Includes one case related to anesthesia.*
**** Includes back pain (8), abdominal pain (1), nausea (1), and vomiting (1).*

The inexperience of the nurse-midwives and the syringe problem resulted in procedure times (from insertion to removal of the speculum) as high as 30 minutes and averaging 18.6 minutes during the first part of this study. However, after the study progressed and new equipment was introduced, the mean procedure time dropped to 7.2 minutes and no procedures performed required more than 10 minutes.

During the study period after February 15, 1975, prophylactic oxytocics were given to 42 percent of the patients. These women experienced significantly fewer instances of delayed fever treated with antibiotics ($p<.05$), and fewer women had delayed complications in general, although this difference was not significant ($p>.05$).

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V. SUMMARY

This study indicates that with adequate training and clinical experience, qualified nurse-midwives can perform menstrual regulation procedures in a safe, effective, and reasonably efficient manner. The experience of these clinics emphasizes the importance of training, both in the actual procedure and in care of the equipment. After the faulty syringes were replaced and the nurse-midwives were given additional training, the nurse-midwives in Isfahan performed 571 menstrual regulations with no immediate complications, no procedure failures, only one incomplete procedure, and an extremely low rate of follow-up complications.

5

EVALUATION OF INTRAMUSCULAR PROGESTERONE FOR THE DIAGNOSIS OF EARLY PREGNANCY

by

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I. INTRODUCTION

The clinical diagnosis of early pregnancy is often difficult, especially within one or two weeks of a missed menstrual period. One approach that has been popular in a variety of countries in recent decades has been the administration of progestational hormones designed to produce "withdrawal" bleeding in cases of "functional" amenorrhea, thus differentiating these cases from pregnancy amenorrhea. To our knowledge, however, the efficacy of this approach to the diagnosis of early pregnancy has never been demonstrated in a controlled study. A previous controlled study of an estrogen-progesterone injection revealed that combination to be ineffective as a hormonal pregnancy test . The present study was undertaken to test the efficacy of administering progesterone alone for the early diagnosis of pregnancy.

II. MATERIAL AND METHODS

Women presenting themselves to the outpatient Obstetric and Gynecology Clinic of Kandang Kerbau Hospital in Singapore because of a recently missed menstrual period and requesting evaluation and termination of a suspected early pregnancy were eligible for admission into the study if they met the following criteria: 1) no preexisting medical or gynecological conditions; 2) regular menstrual cycles within a range of 21 to 35 days; 3) no more than 14 days past the expected date of menstrual onset; and 4) no immediate request for use of IUDs or oral contraceptives (or willingness to wait until completion of the study period to initiate OC or IUD use). From March to May 1976, 296 patients consented to participate in the study after the experimental design had been explained to them. The physician opened a sealed envelope containing a random allocation card which assigned the

patient to either a treatment or a comparison group. One hundred and forty-eight patients in the treatment group received an intramuscular injection of 100 mg of progesterone in oil, while 143 patients in the comparison group received no hormonal injection. (Five patients in the comparison group who subsequently decided to continue their pregnancies were withdrawn from the study after the diagnosis of pregnancy was made.) At the time of the initial visit and again on two follow-up visits, a Pregnosticon Dri-Dot pregnancy test was taken.

Each patient returned for her first follow-up visit 10 days after the initial clinic visit. If menstruation had occurred, vacuum aspiration was not routinely performed. At this visit, the subject was reexamined and the pregnancy test repeated. Vacuum aspiration was performed if the patient was still amenorrheic. If the uterus was aspirated, the contents were submitted for pathological examination. The presence of chorionic villi, trophoblast, fetus, amnion, or chorion was considered definite evidence of pregnancy.

All the patients were requested to return for a second follow-up visit two to four weeks later. One hundred percent of the patients returned for the first follow-up visit. For the second follow-up visit, the return rates were 100.0 percent in the treatment group and 97.2 percent in the control group.

III. RESULTS

There were no significant socio-demographic differences between treatment and comparison groups. The mean age and parity in the treatment group

were 29.2 years and 2.7 live births. For the control group, the comparable figures were 29.3 years and 2.5 live births.

The percent distribution of patients by number of days past their expected onset of menses is shown in Table I. The distributions were similar, as expected on the basis of the randomized protocol. Fourteen patients in the treatment group and 13 patients in the comparison group could not state the exact day of onset of their last menstrual period, but on the basis of physical examination were estimated by the physician to be within 14 days of their expected menses.

Shown in Figure 1 are cumulative percent distributions of uterine bleeding or menstruation for patients who menstruated within 10 days of the initial clinic visit. Examination of the graph reveals that more patients in the comparison group menstruated earlier than those who received progesterone. The rates of menstruation for all women, however, were similar--33.8 percent in the treatment group and 34.9 percent in the control--by 10 days after the initial clinic visit. The different daily rates of menstruation between the two groups did not appear to be related to the number of days that menses had been delayed. Nor was the amount of menstrual flow significantly different ($p>.05$) for the treatment and control groups as shown in Table II. One patient in the treatment group reported spotting which had begun the sixth day after the initial visit. Her pelvic examination, however, was consistent with an early pregnancy and vacuum aspiration was performed. Histologic examination of the aspirated tissue confirmed the diagnosis. Two patients in the control group reported moderate bleeding beginning five days after the initial visit. In these cases also after pelvic examination, aspiration was considered indicated

and microscopic examination of the uterine contents confirmed the diagnosis of pregnancy in both cases.

Patients in the treatment group were significantly more likely ($p<.05$) to report at least one complaint than patients in the control group (57.4% and 35.7%, respectively). Among the specific complaints that were significantly more frequent for the treatment group were nausea, headache, dizziness, and abdominal pain.

Figure 2 is a flow diagram summarizing the results of the study in terms of the initial and follow-up pregnancy tests, uterine bleeding, and the results of histologic examination of the aspirated tissue when menstrual regulation (MR) was performed. There was no significant difference between the treatment and comparison groups in the proportions of women who were pregnant or in the number who subsequently underwent MR (99 or 66.9% in the treatment group and 95 or 66.4% in the comparison group). Thus, the administration of progesterone did not appear to act as an abortifacient.

The utility of using intramuscular progesterone as a means of diagnosing early pregnancy can be compared with that of the Pregnosticon Dri-Dot test in terms of the "false-positive" and "false-negative" rates associated with each of these tests using the histologic examination as the criterion for definite diagnosis. Since failure of progesterone to induce withdrawal bleeding is presumed to indicate pregnancy, the "false-positive" rate associated with its use as a hormonal test of pregnancy was 15.3 percent (15/98) in the treatment group. This rate was lower than the "false-positive" rates associated with the urine pregnancy test at the initial visit (42/173 or 24.3%) but was higher than the 10-day Pregnosticon test (11/161 or 6.9%).

Since MR was not routinely performed among women who had uterine bleeding and negative 10-day Pregnosticon tests, it is more difficult to establish accurately the "false-negative" rates associated with these tests based on histologic criteria done. It should be pointed out, however, that at the final follow-up, no study patients were believed to be still pregnant, based on physical examination and on urine tests. Thus, of the 49 women in the treatment group who had uterine bleeding, only 2 had positive Pregnosticon tests at 10 days and both were found to be pregnant after MR for a "false- negative" rate of 4.1 percent associated with the hormonal pregnancy test. The "false-negative" rates for the Pregnosticon Dri-Dot test were higher--29.3 percent (34/116) at the initial visit and 18.8 percent (6/32) at the 10-day follow-up. It thus appears that the intramuscular administration of 100 mg of progesterone in oil was less likely to lead to an erroneous diagnosis of early pregnancy ("false-positive" diagnosis) at the initial visit but more likely to result in this diagnostic error when compared with the Pregnosticon Dri-Dot test at the 10-day follow-up visit. Compared with the Pregnosticon test at either initial or 10-day visits, the hormonal pregnancy test appeared to have a lower "false-negative" rate (i.e., suggested early pregnancy when the diagnosis could not be confirmed on histologic grounds or subsequent patient follow-up).

IV. DISCUSSION

This study was conducted to evaluate the efficacy of progesterone administration as a "hormonal" pregnancy test. The practice of hormone administration has been widespread for at least the past 20 years, but to our knowledge this is the first controlled study undertaken to evaluate its use for this purpose.

Because of certain limitations in the study design, the findings presented here are not claimed to be "definitive". First, histologic specimens of the uterine contents were not obtained from every patient in the study, but only from those for whom the diagnosis of early pregnancy seemed likely. Thus, the "false-positive" and "false-negative" rates cited here should be taken as approximations only, since it is well known that occult abortion of an early pregnancy can occur. This phenomenon may account to an unknown degree for some discrepancies between tests for pregnancy at the initial visit and subsequent pregnancy tests and/or histologic examinations whenever MR was performed. Second, no placebo injection was administered to women in the comparison group. Thus, the clinical significance of the higher rates of symptoms (nausea, headache, and dizziness) reported by women in the treatment group is open to question.

Despite these limitations in the study design, the data presented here show that, if anything, the administration of intramuscular progesterone may delay the onset of menstrual bleeding when compared with no hormone injection.

When compared with the 10-day Pregnosticon Dri-Dot test, the use of progesterone was more likely to lead erroneously to the diagnosis of early pregnancy ("false-positive" diagnosis). The rationale for use of progesterone as a hormonal test of early pregnancy is that if sufficient endogenous estrogen is present, a progesterone "withdrawal" flow will ensue, provided the patient is not pregnant. Some nonpregnant women may have insufficient estrogen effect (e.g., those with low circulating gonadotrophins or with ovarian failure) or others may have uterine pathology (e.g., Asherman's Syndrome) which might result in the absence of pro-

gesterone withdrawal bleeding, thus accounting in part for "false-positive" hormonal tests. Whatever the pathophysiology involved, the data presented here do demonstrate marked advantage of the progesterone induction of menses as a challenge type of test to diagnose early pregnancy when compared with patient follow-up and later urine testing for chorionic gonadotrophin.

Although the administration of the natural hormone, progesterone, in the early stages of pregnancy has not been associated with subsequent abnormalities of the fetus[2], some clinicians may continue to believe that hormonal testing with synthetic progestins, such as are used for oral administration, may be safely administered to a woman to differentiate pregnancy amenorrhea from other forms of amenorrhea. In fact, if a woman so exposed is pregnant, and desires to continue the pregnancy, then her offspring will be at increased risk of cardiovascular deformities[3,4] and if female, may have masculinization of the external genitalia[5].

In conclusion, we believe that the administration of progesterone, when compared to the readily available immunologic tests for pregnancy, has no clear-cut advantage and carries with it possible disadvantages. For these reasons, the clinical use of progesterone injection for the diagnosis of early pregnancy has been abandoned at the hospital where this study was conducted.

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TITLES AND LEGENDS

Table 1: Title: Number of Days Menses delayed at Time of Initial Clinic Visit

Table 2: Title: Amount of Flow Reported Among Patients Menstruating Within 10 Days After Initial Visit

Figure 1: Title: Cumulative Percent Distribution of Patients Menstruating Within Ten Days of Initial Visit

Figure 2: Title: Flow Diagram of Results

Legend: + = positive

- = negative

MR = menstrual regulation procedure

TABLE I

NUMBER OF DAYS MENSES DELAYED AT TIME OF INITIAL CLINIC VISIT

Days Menses Delayed	Treatment Group *(N = 148)* %	Control Group *(N = 143)* %
1	0.0	1.4
2	1.3	1.4
3	2.7	4.9
4	4.7	4.9
5	5.4	4.9
6	8.8	7.7
7	13.5	14.0
8	7.4	7.7
9	0.0	0.0
10	10.8	8.3
11	8.1	7.7
12	8.8	11.2
13	8.8	7.7
14	10.1	9.1
Unknown	9.6	9.1
Mean	9.1	8.1
S.D.	3.4	3.6

TABLE II

AMOUNT OF FLOW REPORTED AMONG PATIENTS MENSTRUATING WITHIN 10 DAYS AFTER INITIAL VISIT

Amount of Flow	Treatment Group *(N = 50)* %	Control Group *(N = 50)* %
Spotting	6.0	0.0
Mild	16.0	4.0
Moderate	68.0	82.0
Heavy	4.0	0.0
Unknown	6.0	14.0

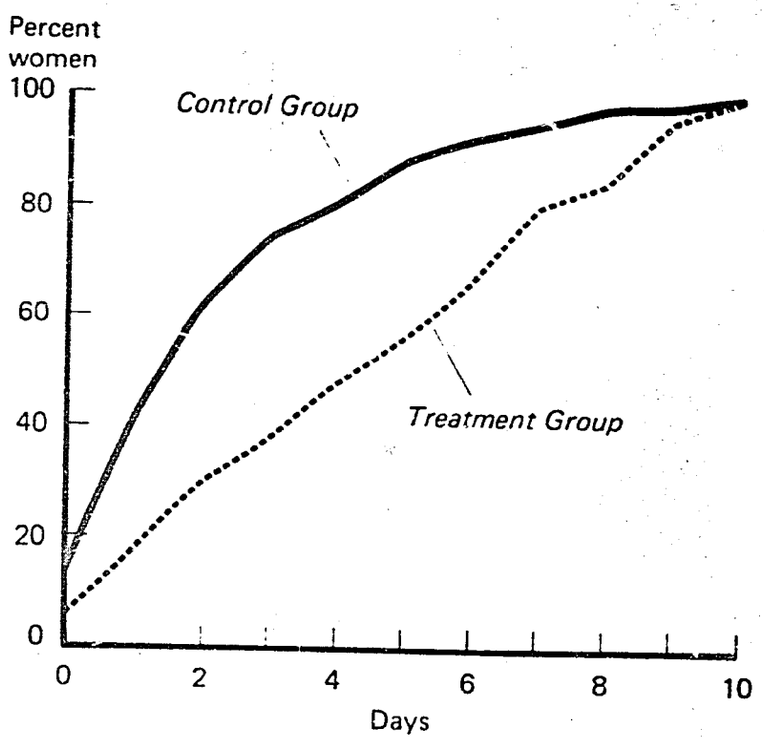

Figure 1. Cumulative Percent Distribution of Patients Menstruating Within Ten Days of Initial Visit.

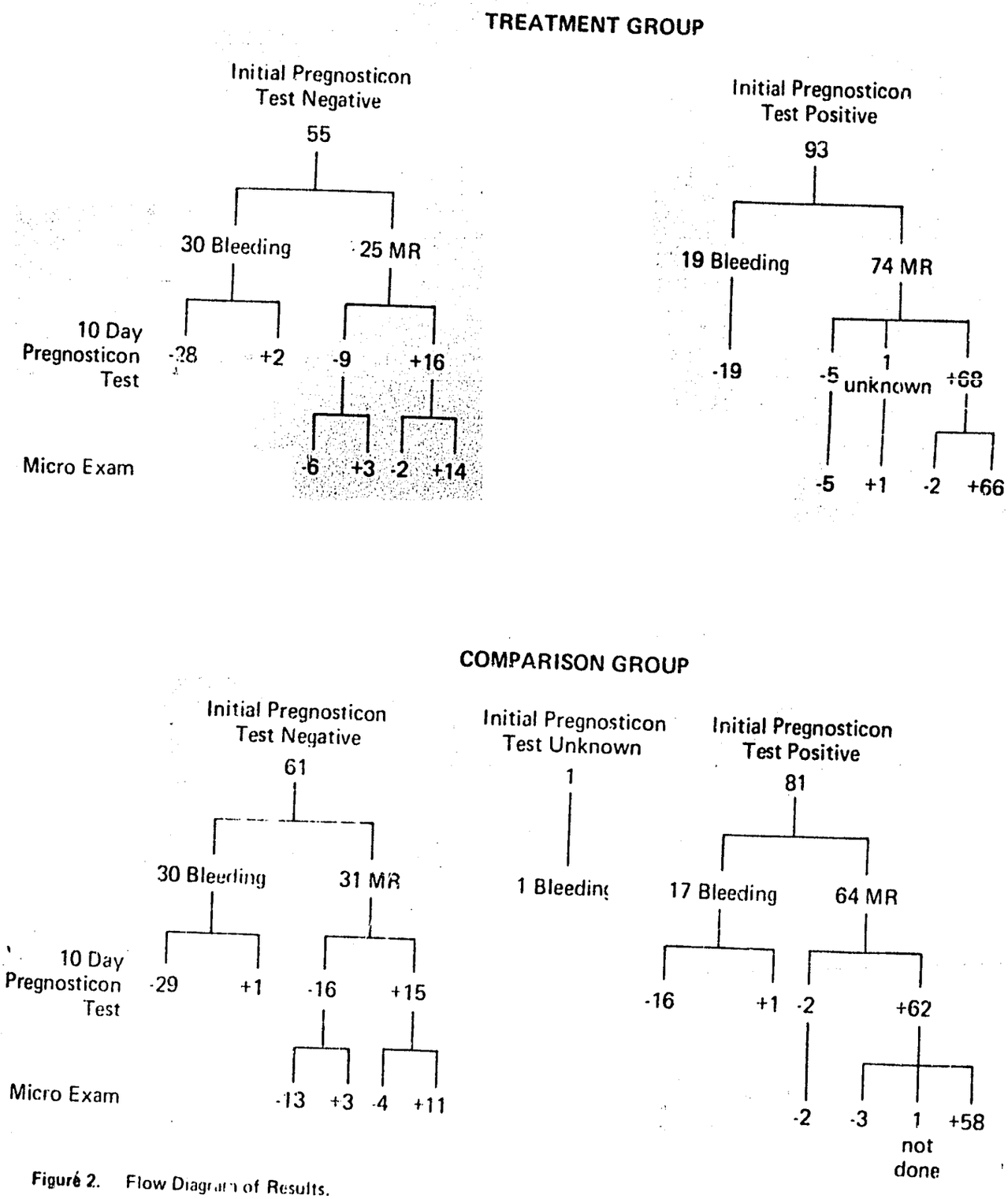

Figure 2. Flow Diagram of Results.

6

MENSTRUAL REGULATION:
UPDATE ON EQUIPMENT, TECHNOLOGY AND THERAPEUTIC USES

By

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INTRODUCTION

Menstrual regulation (MR) is a method for inducing menstruation by aspirating the uterus during the initial four weeks after ovulation, that is within 14 days of the expected onset in menses. The MR procedure is performed by means of a flexible cannula and a suction source. Usually, no cervical dilatation or anesthesia are required. A replacement or alternate vacuum source should be available.

The literature describes voluminous reports of MR procedures performed with minimal difficulty, not only by physicians, but also by paramedics, and even in an unrecommended practice by women themselves. Because of this widespread acceptance, MR is receiving world-wide medical, epidemiologic, legal and ethical attention. There are both humanitarian and health indications for support of MR, particularly in countries where safe induced abortion is illegal. The MR procedure alleviates anxiety in women who are uncertain of their pregnancy by providing them reasonable assurance of a nonpregnant condition before standard relevant tests can be viable, while at the same time relieving their concern about abortion.

The objective of this presentation is to review information available on MR equipment and to discuss the applications of the MR procedure in diagnostic and therapeutic management of patients.

SURGICAL EQUIPMENT

The Cannula

The most frequently used type of cannula is the flexible polyethylene cannula developed by Karman in 1970. It has a rounded tip and two sharp lateral triangular shaped openings located at the distal end on opposite sides of the cannula (Figures 1 and 2). Available in different sizes, starting with a 4 mm diameter, the cannula can be inserted through the cervical os with or without prior dilation of the cervix and with little or no analgesia.

Among the advantages of the Karman cannula is its flexibility, which is believed to reduce the risk of uterine perforation. However, perforation rates for rigid cannula are also low. The instrument is easily sterilized by gas or any sterilizing solution commercially available.

SUCTION SOURCES

Several types of suction can be used including hand, foot and electrically operated equipment.

The Karman Syringe: Figure 3

This is a 50 ml syringe with a plunger displaying sidearm catches to hold it in the fully retracted position. An important feature of the syringe is a valve which permits evacuation of the syringe before beginning the procedure. Since the connecting ends of the cannula and the suction syringe are not of the same caliber, an airtight adapter between the syringe and cannula is needed to bridge the gap. Such adaptors are available to accommodate different cannula

sizes. The syringe is also reusable. Since negative pressure of approximately 60 cm mercury created by the syringe is comparable to the vacuum level of electrically driven pumps, no additional electric power is needed.

The International Fertility Research Program (IFRP) has conducted a study on the current commercially available cannulae and suction syringes to test the durability of the suction syringes using different soaps and sterilizing solutions. The cannulae can be reused for from 21 to 27 procedures. The suction syringe can be reused, without loss of its negative pressure, for from 51 to 84 procedures.

VACUUM SOURCES

Suction Pump

The vacuum capacity of the suction pump is limited because prolonged pumping produces physical fatigue in the operator.

Batelle Negative Pressure Bottle (Figure 4)

In this method, bottles with a capacity of 125 and 250 ccs are used to store vacuum. The bottles are provided with a tissue-collecting bag attached to the cannula entry tube. It is a non-electrical aspirator. The vacuum in the bottle is created by closing the valve, locking approximately 10 ccs of water in the flask, allowing steam to pass out through a check valve and emptying the air in the flask, a process accomplished in 2 minutes' time.

Many variations of the use of the negative pressure bottles or jars are available as an alternative to evacuating pressure bottles by steam condensation.

One such variation is the one shown in Figure 5. It involves the use of stored vacuum bottles evacuated in advance with either an electric pump or a hand vacuum pump. The IFRP is currently evaluating such an approach.

Batelle Hand Pump: Figure 6

The Batelle hand pump is also a nonelectrical, manually operated aspirator. Vacuum is created by 15-20 downward hand strokes of the pump, creating a vacuum of 25-26 inches of mercury. It is provided with a 500 cc collection flask. The IFRP is testing the Batelle hand pump in different clinical settings.

The Burnett hand pump is a commercial version of the Batelle hand pump described above.

The Mity Vac: (Figure 7)

The Mity Vac is a portable, light weight, hand-operated vacuum pump. A vacuum of up to 25 inches of mercury (60 cm) can be attained by a few squeezes of the hand pump. It does not have a collection system, and needs some sort of container or bottle attachment with a double-holed stopper and tubing.

Suction Bulb

This apparatus consists of a cannula, a bottle, and a suction bulb (Figure 8). However, the vacuum level produced by the suction bulb is probably too low to assure complete uterine evacuation.

Water Aspirator

Faucet water aspiration to create bottle vacuum might be adequate, but it is too wasteful of water for use in some communities. Furthermore, the pumping capacity is low and constant control of pressure may be difficult.

NONSURGICAL MENSTRUAL REGULATION APPROACH

The initial use of prostaglandins in menstrual induction was unsatisfactory. The incomplete evacuation of the uterus and the side effects of the medication were unacceptable.

The "Prostaglandin Impact" approach was based on regulatory imbalance due to progesterone withdrawal. Prostaglandin was tested by intrauterine administration of prostaglandin $F_{2\alpha}$ (5 mg) or E_2 (1 mg) pellets transvaginally through an applicator similar to an IUD or by instillation through a catheter over a period of 10-20 minutes. Patients were discharged within four hours. Uterine bleeding followed in three hours, and endometrial tissue fragments were discharged two days later. Spontaneous menses started in 32 days.

Since the number involved in these studies is small, further evaluation of this approach is warranted, especially with the newly available prostaglandin analogues.

Therapeutic Application of MR

Delayed onset of the menstrual period is the major indication for the use of MR. Unless the endometrial aspirate is examined microscopically, an interrupted pregnancy cannot be confirmed. It has been estimated that up to 20 % of the women asking for the procedure were not pregnant. The procedure is safe, simple, and relatively inexpensive and is easily performed in a doctor's office. It offers the advantage of alleviating prolonged anxiety over a possible unwanted pregnancy before pregnancy can be reliably diagnosed; the disadvantage is that some women may undergo the procedure needlessly.

The role of MR in diagnosing various endometrial pathologic conditions has been compared with that of standard dilation and curettage (D&C). In a study by Denis et al ( ) MR and conventional curettage specimens were identical in 97.8 percent of the cases. The only difference observed on microscopic examination was that smaller endometrial fragments were obtained with MR specimens.

Specially designed cannulae are also being tested for abnormal uterine cytology using smears of endometrial aspirate for study. The value of MR as an additional adjunct to screening techniques in high risk patients is already evident. Isaacs et al reported on 346 endometrial aspirations, seven showed endometrial carcinoma ( ).

The role of MR in managing incomplete aseptic and septic abortions and hydatidiform mole early in gestation is documented. However, with more advanced pregnancy or severe uterine bleeding, a large capacity hand pump or electrical backup equipment may be necessary.

The feasibility of providing MR in IUD programs needs to be further explored. Women usually come for IUD insertion during a menstrual period. In high volume clinics, especially with patients coming from far places, it is difficult to avoid inserting IUDs after the safe period. A menstrual extraction prior to IUD insertion in patients in the secretory phase is one solution that may save the patient another trip and still ensure a nonpregnant state.

It has been hypothesized that MR prior to IUD insertion may also result in lower rates of IUD expulsion and removal for bleeding and or pain. This approach is now being examined by IFRP.

In Conclusion

The legal and ethical implications and the ultimate role of MR in the total abortion armamentarium remain to be weighed. In the meantime, immediate and long-term side effects and therapeutic applications are being carefully appraised. For the present, although available equipment is safe and adequate, efforts to improve the equipment and produce it indigenously are continuing.

7

Culdotomy for Female Sterilization

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Introduction

Female sterilization by culdotomy is currently attracting renewed interest in areas of the world where women prefer sterilization by the vaginal route as opposed to abdominal surgery (Wortman[1]). By definition, culdotomy is an incision through the posterior vaginal fornix into the cul-de-sac or pouch of Douglas. Although commonly referred to by the less specific term "colpotomy" (Gr: *kolpos*, vagina; *tome*, incision), culdotomy more accurately describes incision through the posterior vaginal fornix. Incision in the vagina between the cervix and bladder, or anterior colpotomy, has been used in Japan (Adacht[2]), but in most countries culdotomy is the standard technic for performing female sterilization by the vaginal route.

Patient Selection

Sterilization via culdotomy is often more difficult than similar tubal occlusive operations performed via an abdominal incision. Freely mobile pelvic organs and a parous vagina enhance the surgeon's ability to perform the operation successfully. Conditions which interfere with the mobility of the uterus or fallopian tubes, such as pelvic masses or adhesions, or conditions which restrict access to the pelvic organs, such as extreme obesity or a long, narrow vagina, will diminish the likelihood of uncomplicated surgery. Sterilization by culdotomy is often performed at the same time as termination of first trimester pregnancies. After late abortion or term delivery, it should be deferred until uterine involution is complete.

Preoperative Preparation

The minimum preoperative evaluation required for culdotomy includes a medical history and physical examination to identify any conditions which might complicate or contraindicate the procedure, e.g., pelvic mass, adhesions secondary to old pelvic inflammatory disease, endometriosis or pelvic tuberculosis. Routine preoperative laboratory studies include measurement of hemoglobin or hematocrit, urinalysis and Pap smear examination. Preexisting medical or gynecologic conditions such as anemia or genitourinary infection should be treated and resolved before surgery.

The patient should ingest nothing for at least eight hours prior to the procedure, whether the operation is to be performed on an inpatient or outpatient basis. An enema and an antibacterial vaginal douche are usually administered prior to surgery. Immediately before being taken to the operating room the patient should empty her bladder.

Operative Procedure (Fig. 1)

The patient is suitably anesthetized, perferably with general or conduction anesthesia for optimal relaxation and pain relief, and is placed in the dorsal lithotomy position with a slight Trendelenburg tilt. The perineum, vulva and vagina are swabbed with an antibacterial solution such as povidone-iodine and the patient is draped. Pelvic examination is performed to confirm the size, position and mobility of the uterus, which often can be manipulated manually into a retroverted position so that the fallopian tubes lie in the pouch of Douglas.

A speculum is then placed in the vagina in order to expose the cervix and posterior vaginal fornix. The Soonawala speculum, which has a short blade (2-1/2 inches) and a long blade (4-1/2 inches) on opposite ends of the speculum, is a useful instrument. The short blade is used at this stage in the procedure. The cervix is grasped with a tenaculum and is moved gently back and forth in order to identify the bulge of the cul-de-sac between the cervix and the rectum (Fig. 1a). The vaginal mucosa can be lifted at this site with Allis forceps and a single transverse incision made through the vaginal mucosa, submucosal tissue and peritoneum directly anterior to the forceps (Fig. 1b). Repeated timid attempts at dissection through the vaginal submucosa and peritoneum may cause unnecessary bleeding. The incision into the peritoneal cavity can then be extended laterally by removing the Soonawala speculum from the vagina and reinserting it, long blade first, through the culdotomy incision. Similarly, it can be extended with blunt or sharp dissection, being careful not to incise the uterosacral ligaments. A small, tagged, moist pack can be inserted to push any loops of bowel out of the way.

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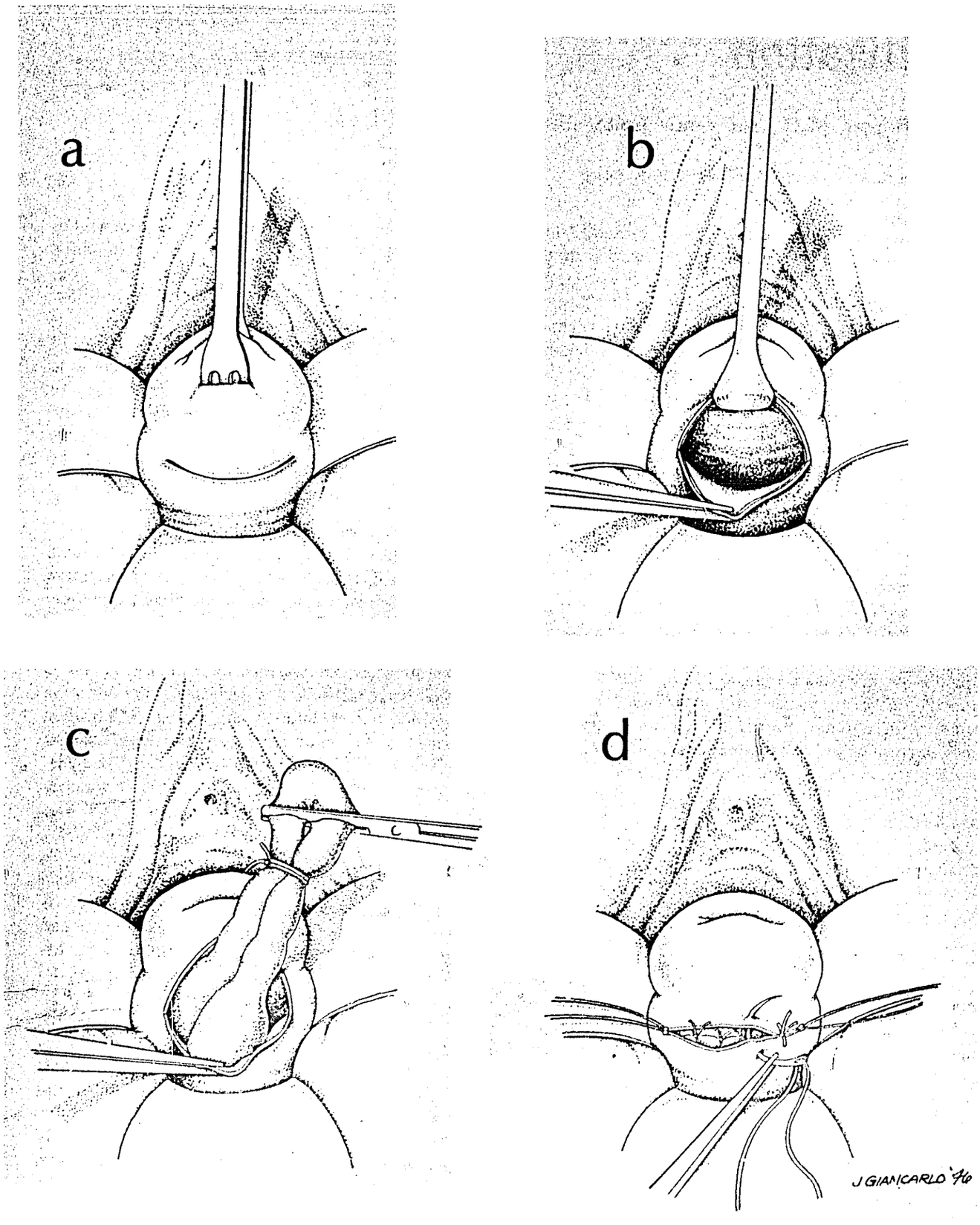

FIGURE 1. — Technic for performing culdotomy.

TABLE 1. — Major Complications of Sterilization by Culdotomy

Complication	Selected Studies* (N = 5,123) Number	Percentage	IFRP Data (N = 1,043) Number	Percentage
Bowel/Bladder Injury	7	0.1	3	0.3
Pelvic Hematoma	6	0.1	3	0.3
Other Hemorrhage	34	0.7	10	1.0
Pelvic Abscess	13	0.3	2	0.2
Other Infection	115	2.2	40	3.8
Total	175	3.4	58	5.6

*Source: Reference 2, Table 6.

The pelvic organs are then visualized. If the uterus is not retroverted, it can be repositioned with an intrauterine sound or the fundus can be grasped and pulled posteriorly with a hook. One fallopian tube at a time is grasped with a Babcock clamp and pulled through the incision (Fig. 1c). If the fallopian tube cannot be easily identified, it can often be pulled into view by applying traction to the uterosacral ligament.

The precise technic of tubal sterilization may be selected from a variety of procedures, including tubal occlusion with suture, clips or bands with or without crushing, dividing, or cauterizing. Specific procedures which have been recommended include fimbriectomy, Pomeroy ligation, modified Pomeroy, and Madlener technics. The modified Pomeroy technic appears to be the most satisfactory based on analyses of method-specific failure rates and complication rates (Brenner[3]).

After tubal sterilization has been completed, each fallopian tube must be carefully inspected to verify occlusion of the correct structure and maintenance of adequate hemostasis. After replacing the tubes in the peritoneal cavity, the culdotomy incision is closed with absorbable suture, preferably in a single layer (Fig. 1d). If additional dissection was needed to enter the peritoneal cavity, the peritoneum and vagina will be separated and must be closed in separate layers.

Adequate time is needed for complete recovery from anesthesia (at least two hours for general and eight hours for spinal). During this time period, observations of the vital signs and of any vaginal bleeding will alert the surgeon to any intraperitoneal or vaginal bleeding. Sexual intercourse should be avoided until follow-up examination in four weeks shows normal wound healing.

Complications and Failures

Similar to other intrapelvic operations, the most frequent medical complications of sterilization by culdotomy are hemorrhage, infection and injury to structures other than the fallopian tubes. Major complication rates associated with over 5,000 operations were reviewed in detail by Wortman and Piotrow[1] and are summarized in Table 1. This table also shows the major complications reported in 1,043 interval (i.e., not postabortal or puerperal) culdotomy sterilizations performed in a five year period by 21 contributors to the International Fertility Research Program (IFRP). Criteria of "major" complications may vary in previously published series but for the IFRP data "other hemorrhage" includes bleeding (other than pelvic hematoma) that results in shock or requires blood replacement and "other infection" includes patients with pelvic cellulitis, endometritis, peritonitis, salpingitis, urinary tract infection or febrile complications that were treated with antibiotics even without a specific diagnosis. Despite some variation in the specific complication rates between the two series, clearly infection (excluding pelvic abscess) is the most common complication followed by hemorrhage (excluding hematoma). Bowel or bladder injuries, pelvic hematomas and abscesses also occurred.

Sometimes, the intended sterilization procedure cannot be performed successfully by the vaginal route. The most frequent reason for failure was pelvic or tubal

TABLE 2. — Reasons for Failure to Complete Sterilization by Culdotomy

Reason	Selected Studies* (N = 5,267) Number	Percentage	IFRP Data (N = 1,043) Number	Percentage
Adhesions	21	0.4	9	0.9
Obesity	6	0.1	0	—
Bowel Injury/Repair	0	—	2	0.2
Difficulty Opening Peritoneum	0	—	2	0.2
Other	3	0.1	3	0.3
Unspecified	6	0.1	0	—
Total	36	0.7	16	1.5

*Source: Reference 2, Table 5.

adhesions (Table 2). In the earlier series, obesity was the second most common reason for failure. In two of the three cases of bowel injury reported to the IFRP, laparotomy was required for bowel repair and completion of the sterilization operation. Difficulty in entering the peritoneal cavity via the vaginal route led to abdominal sterilization in two other IFRP cases. The category "other" in the published studies includes one case each of avulsion of a fallopian tube, inability to reach the tubes and coagulation of the round ligament. In the IFRP studies, "other" includes laparotomies for two ovarian cystectomies and one myomectomy in cases where the nature of the pathologic condition was appreciated only after culdotomy had already been performed.

Conclusion

Permanent female sterilization may be accomplished through a culdotomy incision. Under some circumstances and for selected women, this approach may be more acceptable than abdominal sterilization procedures. However, the technic requires that the surgeon be highly skilled in performing vaginal surgery. The incidence of major immediate complications is higher than for tubal sterilization performed either by laparotomy or laparoscopy.[3]

Currently available information regarding culdotomy is based on retrospective controlled series; however, comparative studies are being undertaken to evaluate more accurately the advantages and disadvantages of female sterilization via culdotomy, culdoscopy, laparotomy and laparoscopy. So far, culdotomy does not appear to offer the advantages of technical ease and safety which are sought in the "ideal" sterilization method that can be applied by general medical or professionally trained paramedical personnel in any country in the world.

Summary

Tubal occlusion through a culdotomy incision offers a method of surgical sterilization acceptable to women in some countries where abdominal sterilization is not acceptable. This technic requires skilled gynecologic surgeons, who are a limited resource in many developing countries. On the other hand, gynecologic surgeons practicing in outlying areas may find it more feasible to perform colpotomy sterilizations than laparoscopic sterilizations with the latter's requirements for specialized instrumentation and additional training.

With adequate attention to operator training, patient selection, evaluation of patients for postoperative complications and appropriate care of those with such complications, culdotomy should be included among the various approaches appropriate for female sterilization.

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EXPERIENCE WITH MINILAPAROTOMY IN THE PHILIPPINES

Running Head: Experience with minilaparotomy

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Abstract

This paper presents the socio-demographic characteristics, medical histories, and clinical data on 651 interval minilaparotomy sterilization procedures performed in Manila, Philippines. About two thirds of the procedures were performed with local anesthesia; the Pomeroy technique was used for tubal ligation. In 2.8% of the patients, salpingectomy or fimbriectomy was performed on one side because of surgical difficulties and complications. Surgical difficulties were encountered in 19.8% of the procedures; adhesions (4.3%) and bowel interference (4.0%) were the most frequent causes of surgical difficulty. Complications occurred during surgery in 1.7% of the procedures. Early post-operative complications were noted in 9.1% of the cases. None of the patients required readmission to the hospital. While 612 women were followed up at 6 months, 299 were followed up at 12 months. One woman (0.2%) became pregnant after sterilization; at repeat minilaparotomy, ligation of the last round ligament rather than the tube was observed. Pelvic surgery, other than pregnancy-related surgery, during the year following sterilization was reported for one patient who underwent exploratory laparotomy with appendectomy and oophorociptectomy. Menstrual pattern changes are also discussed. The results of this study suggest that tubal ligation via minilaparotomy is practical, safe, and effective.

I. INTRODUCTION

Female sterilization is rapidly becoming one of the most important methods of family limitation. In the Philippines, this method of fertility control is given a heavy emphasis at the national level. Several important advances have taken place in the last decade to make female sterilization a safe, simple, low cost, widely applicable procedure. The aim is to take this method to rural populations which have the greatest need for limiting family size. While endoscopic methods have the advantage of minimizing hospital stay and cost, they carry certain inherent disadvantages which make it difficult for developing countries to use these methods, particularly in rural areas. Lack of trained physicians and maintenance of expensive equipment are the main problems with laparoscopic techniques. Physicians in developing countries are, therefore, striving to find suitable methods of female sterilization which would be safe, simple, acceptable, inexpensive, and widely applicable under local conditions.

Minilaparotomy is a promising technique that is being increasingly used in developing countries, notably in Thailand, the Philippines, and India. Special endoscopic training and equipment are not necessary and the procedure can be adapted to various conditions, depending on the local availability of medications and equipment. The present paper reports the findings of a study conducted in the Philippines to evaluate the safety and feasibility of this technique.

II. MATERIALS AND METHODS

Minilaparotomy procedures performed from May 3, 1974, to June 17, 1975, at the Comprehensive Family Planning Centre of the José Fabella Memorial Hospital in Manila, Philippines, are reported in this paper. Data on the socio-demographic characteristics, medical history, sterilization procedures, and associated complications for 651 interval cases were reported by the two senior authors on standard forms of the International Fertility Research Program. These data were processed and analyzed by the other two authors. In this study, the patients were followed up 7 to 21 days, 6 months, and 12 months after sterilization.

Subjects

Only women who were sterilized for the purpose of limiting family size were included in the study. Previous abdominal and pelvic surgery were reported for 7.9 and 1.3% of the patients respectively.

Clinical Procedures

The patient was counseled and medically evaluated. For this technique of female sterilization, it is important to ensure that the uterus is mobile. Uterine mobility was tested with the aid of the uterine elevator developed at the Ramathibodi Hospital, Bangkok, Thailand (Fig. 1). This instrument is a uterine sound provided with a collar fixed at a distance of 4 cm from the rounded tip to prevent uterine perforation. The uterus was gently elevated towards the anterior abdominal wall until actual bulging was observed. If no bulging was seen, this indicated that the uterus was not sufficiently mobile and minilaparotomy was not

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performed. Testing for uterine mobility is important with this method because, if the minilaparotomy procedure has been started and pelvic adhesions make it difficult to expose the tubes, the incision must then be enlarged.

The patient was advised to take a laxative orally or in suppository form the night before surgery was scheduled. She was advised to come to the hospital with an empty stomach. A hypodermic injection containing 50 mg of meperidine, 5 mg of diazepam, 25 mg of promethazine, and 1/150 gr of atropine was administered as premedication 30 minutes before surgery. The pubic hair was shaved and the abdominal wall cleansed with soap and water. A 5% saline infusion was started and continued throughout surgery. The patient was placed in the lithotomy position, and a pelvic examination was performed. A vaginal speculum was inserted, and the cervix cleansed with povidone-iodine or hexachlorophene. The anterior lip of the cervix was grasped with the tenaculum and the uterine elevator inserted; the tenaculum and speculum were removed once the elevator was positioned and uterine mobility retested. The bladder was completely emptied and the operative field prepared with povidone-iodine. An operative area 2 x 3 inches was exposed through the sterile drapes just above the symphysis pubis. The patient was then placed in the marked Trendelenberg position.

About two thirds of the sterilization procedures (63.0%) were performed under local anesthesia; 15 to 20 ml of mepivacaine hydrochloride were injected in all the layers of the abdominal wall. In 55.5% of the cases, local anesthesia was combined with neuroleptanalgesia;

50 mg of meperidine and 10 mg of diazepam were administered intravenously just before giving local anesthesia. Regional anesthesia was used for 32.1 and general anesthesia for 4.0% of the procedures.

A 1-inch transverse incision was made 1 inch above the symphysis pubis and the subcutaneous tissue bluntly dissected with a round-nose forceps. An incision of the fascia was then made with a scalpel and enlarged with scissors; the muscles were next separated bluntly. When the peritoneum came into view, the assistant directed the uterine fundus towards the incision and the peritoneum was carefully lifted, taking extreme care not to include a loop of the intestine or the bladder wall. (This is the primary potential danger of this technique). The peritoneum was then opened and the uterus brought into view by applying the small retractors. By further tilting the uterus to one side, the tube was brought into view. The tube was then picked up lightly with a forceps and its fimbriated end exposed for absolute indentification. It was ligated and cut using the original Pomeroy method. The peritoneum was then closed by a purse-string suture and the fascia by a figure-of-eight suture. One suture was applied to the subcutaneous tissue, the skin was closed, using a subcuticular stitch, and a small dressing was applied. (For a list of instruments required for this procedure, see Appendix.)

The patient rested for 3 to 4 hours before being permitted to go home, but most of them preferred to stay overnight. Aspirin tablets were recommended for pain. The patient was informed that sexual abstinence was unnecessary. A postoperative visit was scheduled 21 days after surgery when a pelvic examination would be performed to detect any complications.

Since this study was completed, many changes in medications and operative technique have been introduced to further simplify the operation. These changes will be described in the addendum.

III. RESULTS

Patient Characteristics

Table I shows the age by parity distribution of patients in the study. The mean age of the patients was 32.9 years and their mean parity was 5.5. The mean number of living children was 5.1; two thirds of the women (57.8%) had five or more living children. Most of the patients as well as their husbands had received formal education, with the mean number of completed school years being 8.3 and 9.4, respectively. Half of the patients (53.1%) were from Manila or another urban area and half (46.9%) were from rural areas.

While 20.0% of the women had not used any method of fertility control during the three months prior to surgery, about an equal proportion had used orals (34.6%) and IUDs (31.8%).

Technical Failures

Technical failures were defined as cases in which the procedure could not be completed as planned. There were no cases in which tubal occlusion was not accomplished. However, in 18 (2.8%) patients the Pomeroy technique was not used on one side and salpingectomy or fimbriectomy of the tube was instead performed. Bleeding or tearing of the tube (8 cases) were surgical complications for which the sterilization

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technique had to be changed to partial salpingectomy. Seven patients had ovarian cysts that were removed with the fimbrial end of the tube. Adhesions presented a problem in two cases and a thickened tube in one case, necessitating partial salpingectomy. These difficulties and complications during surgery are included with other difficulties and complications in Tables II and III.

Difficulties at Surgery

Table II shows that difficulties were encountered during surgery in 19.8% of the procedures. Adhesions (4.3%) and bowel interference (4.0%) were the most frequent difficulties. In 2.6% of the procedures, the surgeon experienced some difficulty in opening the peritoneum and in 2.3% in identifying and ligating the tube. Inadequate anesthesia was responsible for difficulties in 2.0%, and a retroverted uterus presented some difficulty in 1.7% of the patients.

Surgical Time and Hospitalization

The average time from incision to closure was 25.3 minutes for patients who did not undergo other surgery. The vast majority of the patients were hospitalized for one night only.

Operative and Immediate Postoperative Complications and Complaints

Complications occurred during surgery for 11 (1.7%) patients. In nine cases there was tearing or bleeding of the tube, in one case the bladder was injured during surgery, and in one case the uterus was perforated (Table III). The bladder and uterine injuries were both repaired surgically through the minilaparotomy incision. Immediate

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postoperative complications (i.e., those occurring between surgery and discharge) were not reported for any patients.

Table IV shows that pain at the operation site (41.3%) was the most frequently reported immediate postoperative complaint. Anesthesia-related complaints were noted for 28 patients (4.3%); of these, 27 had headache due to spinal anesthesia and 1 had vomiting.

Early Postoperative Complications and Complaints

Early postoperative complications were noted during the period between hospital discharge and the 7-to-21 day follow-up visit for 57 (9.1%) of the 623 cases seen for follow-up (Table V). Forty-six of these patients had wound complications. Infection of the urinary tract was reported in three patients: pyelonephritis in two of them (0.3%) and cystitis in one (0.2%). Of these patients, one had a history of urinary infection and another was the woman whose bladder was injured during the sterilization procedure. All three were successfully treated with antibiotics. In this series, nine patients (1.4%) had fever requiring antibiotics. None of the patients in the study group required re-admission to the hospital.

Incision or pelvic pain (8.8%) and gastro-intestinal problems (3.4%) were the most frequently reported early postoperative complaints (Table V). Nineteen % of the patients returning for follow-up had one or more complaints.

Late Postoperative Complications and Complaints

Of the 651 patients included in the study, 412 were observed at 6 months and 299 at 12 months. One woman (0.2%) became pregnant after sterilization; at repeat minilaparotomy, ligation of the left round ligament, rather than the tubes was observed. Another woman's pregnancy was documented after sterilization, but review of her history showed that she has been pregnant at the time of surgery. Pelvic surgery, other than pregnancy-related surgery, during the year following sterilization was reported for one patient, who underwent exploratory laparotomy with appendectomy and left oophorociptectomy. Pelvic or back pain was reported by 3.3% of the patients seen at the 6-month visit and by 2.4% of the patients seen at the 12-month visit, but in no case was the pain believed to be related to sterilization.

Menstrual pattern changes were also analyzed for those patients who had not been using systemic contraceptive or intrauterine devices before sterilization. This group of patients included 140 woman seen at 6 months and 106 women seen at 12 months postoperatively. Menstrual cycle regularity had not changed from 72.3% of the patients at 6 months and for 75.0% of the patients at 12 months; a change from regular to irregular cycles was reported by 21.8% at 6 months and by 16.0% at 12 months, while a change from irregular to regular cycles was reported by 5.9% and by 9.0% respectively. Of the women whose menstrual cycle was regular both before and after sterilization, menstrual cycle length had not changed by more than one day for approximately 98% at 6 and 12 twelve months postoperatively. Among approximately three fourths of the women, the duration of menstrual flow had not changed by more than one day at

either time period; most of the women experiencing a change had shorter durations of flow. "Normal" amount of flow was reported by approximately 80% of the patients both before and after sterilization. Dysmenorrhea either remained the same or decreased for all except about 20% of the patients who had no dysmenorrhea before sterilization but complained of mild dysmenorrhea at the time of follow-up.

IV. DISCUSSION

The search continues for methods of female sterilization which could be applicable on a large scale especially in rural areas of developing countries. The abdominal approach for interval female sterilization has been widely used, but a large abdominal incision is associated with prolonged hospitalization and incapacitation. By using a small incision, the procedure is quicker and is associated with less operative trauma and, therefore, with minimal hospital stay and cost. While laparoscopic methods have also been successful in this respect, they have several built-in limitations which have hindered their large scale application in developing countries. Minilaparotomy, on the other hand, because it requires standard operating room equipment and can be performed by surgeons with no sophisticated training, seems to have a distinct value for large scale programs.

Physicians in Thailand have been using minilaparotomy extensively for several years. The overall rates of complications have been low, but potentially serious complications, including uterine perforation and bladder injury, do occur (3,4,5,7). It is hoped that modifications in

the instrument used for uterine elevation will preclude the problem of inadvertant uterine perforation, while greater care in making the incision should prevent bladder injury. These complications were primarily noted early in the minilaparotomy program and can be expected to decline as the technique is perfected and experience is gained in the performance of the procedure.

The Profamilia program in Colombia has also reported a large series of patients sterilized by minilaparotomy procedures performed on an ambulatory basis in a family planning clinic building (6). No serious complications were noted in the first 600 patients.

A small randomized study of outpatient sterilization by laparoscopic electrocoagulation and minilaparotomy with the Pomeroy method of tubal occlusion conducted at the Johns Hopkins Hospital demonstrated no serious complications in either group (2). However, laparoscopy presents inherent danger as an endoscopic technique, with these dangers compounded by the widespread use of electrocoagulation as the tubal occlusion technique.

In a recent analysis of all IFRP data of laparoscopy and minilaparotomy procedures performed for women who had not recently been pregnant (1), the surgical complication rate was low (approximately 2% for each group). The theoretically lower complication rate of the simpler minilaparotomy procedure was not realized, probably due in part to the fact that the reported minilaparotomy procedures represented the early learning experience with minilap of many of the surgeons involved. The serious complications of minilaparotomy, although infrequent, point to

the need for a careful training of physicians if this procedure is to achieve the desired level of safety.

Studies such as the one reported in this paper are demonstrating that the minilaparotomy technique is associated with clinically acceptable rates of complications. Tubal trauma and bleeding were reported for nine cases (1.4%) and bladder injury and uterine perforation were each sustained by one patient (0.2%). While these complications also occur during laparoscopic procedures, they are more readily diagnosed and treated via minilaparotomy. When any of these complications occur during laparoscopy, laparotomy is often required, either concurrent with laparoscopy or at a later time if the complication is not recognized immediately. The problem of delayed diagnosis of the complication is particularly critical in cases of bowel injury with accompanying peritonitis.

The results of this study contribute to the increasingly accepted belief that minilaparotomy with tubal ligation is the technique which can today be offered practically, safely, and effectively to the greatest number of women throughout the world.

ADDENDUM

From the date of completion of this study in June 17, 1975 to December 31, 1976, 1,837 more minilaparotomies were performed. Additional experiences and the continuous search for further simplification of the procedure have enabled us to dispense with some steps in the preparation of the patient and in the operative procedure described in this report.

The prescription of a laxative or a suppository and the advice to come in on an empty stomach are given only to the few patients who are willing to postpone surgery to a later date. The majority of patients just walk into the clinic and are immediately operated on after the usual clearances. For this group, no previous preparations are made.

Likewise, the premedication with meperidine, diazepam, promethazine hydrochloride, aand atropine administered 30 minutes before surgery has been stopped. Patients walk to the operating room. Once on the operating table, dextrose infusion is started and meperidine 75 mg with diazepam 5 mg is given. The patient is then prepared for surgery and the operation started, using 10 cc of local mepivacaine hydrochloride or lidocaine anesthesia.

In the operative procedure, the surgeon now performs the uterine elevation himself. By so doing, he can manipulate the uterus to the position he desires.

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APPENDIX

Instruments Required

20 cc syringe and needle for local anesthesia

Pair of small retractors

Knife

Two round-nose (6- or 8-inch) forceps

6-inch pick-up toothed forceps

6-inch curved scissors

Pair of 6-inch straight scissors

Needle holder

Uterine elevator

6-inch straight forceps

Needles and catgut

TITLES AND LEGENDS

Tables I - V:	Titles on tables.
Figure 1:	Title on figure.

TABLE I

AGE BY PARITY DISTRIBUTION OF 651 WOMEN STERILIZED BY MINILAPAROTOMY AT DR. JOSE FABELLA MEMORIAL HOSPITAL MANILA, PHILIPPINES, MAY 1974–JUNE 1975

	Age							
	30		30-34		35+		Total	
Parity	No.	%	No.	%	No.	%	No.	%
2-4	97	14.9	101	15.5	40	6.1	238	36.6
5-6	53	8.1	92	14.1	92	14.1	237	36.4
7 or more	9	1.4	60	9.2	107	16.4	176	27.0
Total	**159**	**24.4**	**253**	**38.9**	**239**	**36.7**	**651**	**100.0**

TABLE II

DIFFICULTIES AT SURGERY FOR 651 WOMEN STERILIZED BY MINILAPAROTOMY AT DR. JOSE FABELLA MEMORIAL HOSPITAL MANILA, PHILIPPINES, MAY 1974–JUNE 1975

Difficulty at Surgery	No.	%
Adhesions	28	4.3
Bowel interference	26	4.0
Difficulty in opening peritoneum	17	2.6
Difficulty in ligating the tubes	15	2.3
Inadequate anesthesia	13	2.0
Retroverted uterus	11	1.7
Ovarian cyst	7	1.1
Difficulty in locating tubes	5	0.8
Difficulty in closing peritoneum	4	0.6
Obesity	3	0.5
Total	**129**	**19.8**

TABLE III

OPERATIVE COMPLICATIONS OF 651 PATIENTS STERILIZED BY MINILAPAROTOMY AT DR. JOSE FABELLA MEMORIAL HOSPITAL MANILA, PHILIPPINES, MAY 1974–JUNE 1975

Complication	No.	%
Tear/bleeding of tube	9	1.4
Bladder injury	1	0.2
Uterine perforation	1	0.2
Total	**11**	**1.7**

TABLE IV

IMMEDIATE POSTOPERATIVE COMPLAINTS OF 651 PATIENTS STERILIZED BY MINILAPAROTOMY AT DR. JOSE FABELLA MEMORIAL HOSPITAL, MANILA, PHILIPPINES, MAY 1974–JUNE 1975

Complaint	No.	%
Pain at operative site	269	41.3
Anesthesia related complaints		
Headache	27	4.1
Vomiting	1	0.2
Total	28	4.3
Syncope/dizziness	12	1.8
Gastrointestinal complaints	6	0.9
Dysuria	1	0.2
Tympanism	1	0.2
Vaginal bleeding	1	0.2
Shoulder pain	1	0.2
Women With One or More Immediate Postoperative Complaints	**310**	**47.6**

TABLE V

EARLY POSTOPERATIVE COMPLICATIONS AND COMPLAINTS OF 623* PATIENTS STERILIZED BY MINILAPAROTOMY AT DR. JOSE FABELLA MEMORIAL HOSPITAL, MANILA, PHILIPPINES, MAY 1974–JUNE 1975

Complications	No.	%
Wound complications	46	7.4
Stitch abscess	25	4.0
Wound drainage	12	1.9
Wound infection	2	0.3
Bleeding from wound	2	0.3
Wound hematoma	1	0.2
Wound gaping	4	0.6
Fever requiring antibiotics	11	1.8
Pyelonephritis	2	0.3
Cystitis	1	0.2
Women With One or More Early Postoperative Complications	**57**	**9.1**
Complaints		
Incision/pelvic pain	55	8.8
Gastrointestinal complaints	21	3.4
Syncope/dizziness	12	1.9
Headache	11	1.8
Dysurea/urinary frequency	10	1.6
Vaginal discharge/bleeding	6	1.0
Tympanism	1	0.2
Women With One or More Early Postoperative Complaints	**116**	**18.6**

* *Twenty-eight patients did not return for their 7–21 day follow-up visit.*

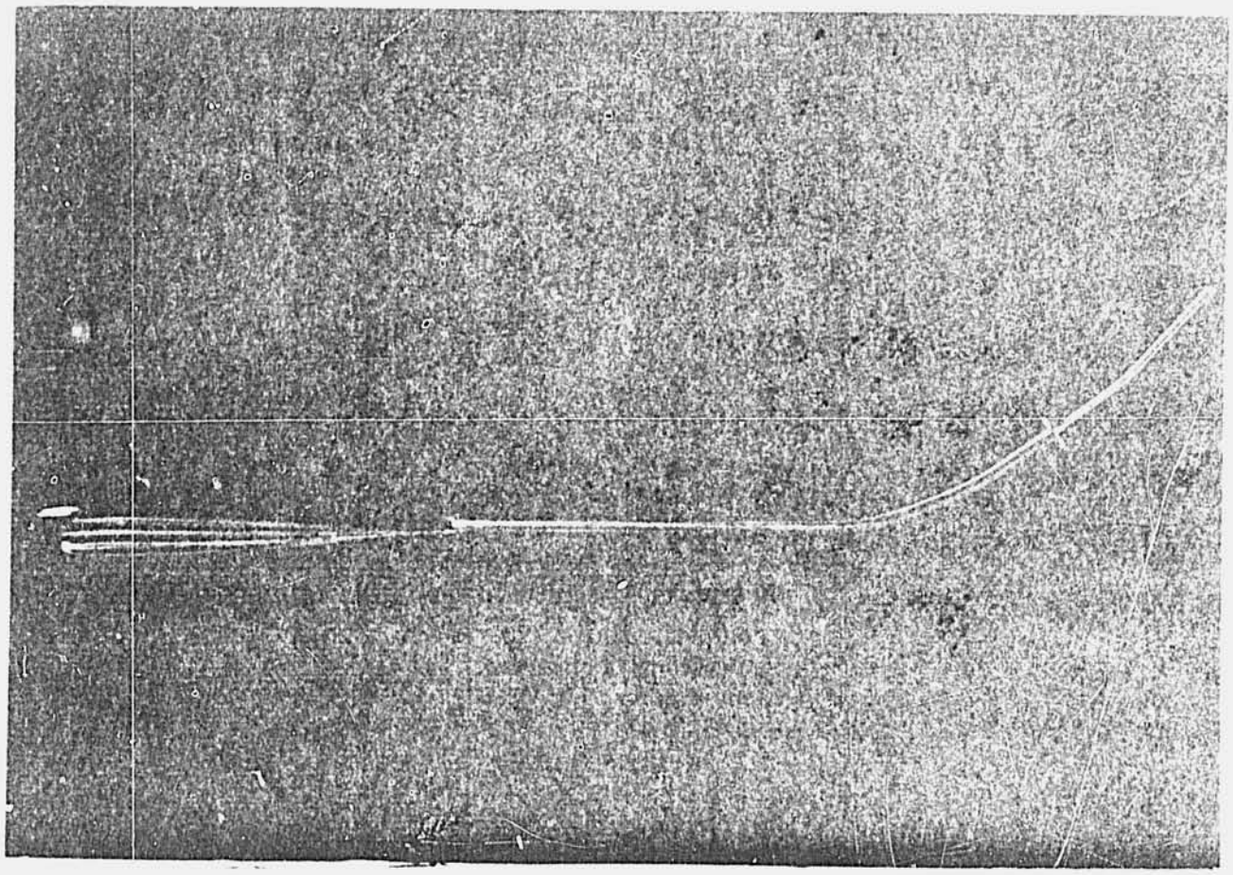

Figure 18. Uterine Elevator

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FEMALE STERILIZATION SERIES
NO. 77

INTERNATIONAL FERTILITY RESEARCH PROGRAM
CONFERENCE PAPER

LAPAROSCOPIC ELECTROCOAGULATION AND TUBAL RING TECHNIQUES FOR STERILIZATION — A COMPARATIVE STUDY

By

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LAPAROSCOPIC ELECTROCOAGULATION AND TUBAL RING TECHNIQUES FOR STERILIZATION--A COMPARATIVE STUDY

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I. INTRODUCTION

Laparoscopic female sterilization is a relatively safe, short operation with minimal complications and low mortality[1]. In addition, it can be performed as an outpatient procedure using local anesthetics.

The standard laparoscopic technique of tubal occlusion has been that of electrocoagulation with unopolar forceps. The risk of burns to the bowel and other organs, although small[2], has led to the development of bipolar electrocoagulation forceps[3] and such nonelectrical occlusive devices as the clip[4] and the tubal ring[5]. Theoretically, the newer mechanical devices should be safer for the patient and increase the chances of reversibility since a smaller portion of the tube is damaged.

This study evaluated the safety, effectiveness and ease of performance, of laparoscopic sterilization by the tubal ring technique as compared with standard electrocoagulation.

II. METHODS AND MATERIALS

From August 1975 through May 1976, a comparative study of standard electrocoagulation and application of the tubal ring for tubal occlusion was conducted at the Siraraj Hospital in Bangkok, Thailand. Data from this study were recorded on standard forms designed to obtain information on selected sociodemographic characteristics of the patients, the medical aspects of the sterilization procedures, and complications and other events occurring from the time of surgery to 12 months after sterilization.

Study Design

The two techniques were randomly assigned to 300 patients. One operator performed all surgical procedures; another physician, who was unaware of the specific technique performed, provided postoperative and follow-up care. All procedures were performed on an outpatient basis for women who had not recently been pregnant. Only women requesting sterilization for family planning purposes were included in the study. Patients were scheduled for three follow-up visits after surgery: at 7 to 21 days, 6 months, and 12 months.

Equipment

The tubal ring (Figure 1) is a 2 mm-thick band of siliconized rubber with an inner diameter of 1 mm and an outer diameter of 3.6 mm. A specially designed tubal ring applicator with grasping forceps (Figure 2) is used in the application of the ring to the tube.

The monopolar Electrocom 120 manufactured by Martin Bicomatic is the unit used for electrocoagulation.

Sterilization Procedures

Prior to sterilization, a complete medical history, physical and pelvic examinations, and laboratory tests, including chest x-ray, urinalysis, hematocrit, and Papanicolaou smear, were done for each patient. The patient was instructed to give herself an enema on the morning of the operation, to clean her umbilical area thoroughly, and to come to the hospital without breakfast. She voided immediately before surgery. A combination of 100 mg of pethidine and 2.5 mg of droperidol was administered intravenously about 10 minutes before surgery (the dose was adjusted slightly for markedly overweight or underweight patients).

After the patient was prepared for surgery, draped and in the Trendelenberg position, 10 to 20 ml of 1% lidocaine was injected into the abdominal wall immediately subumbilically. Pneumoperitoneum was created with one to two liters of carbon dioxide. Both study procedures were performed via a single incision.

When electrocoagulation was the assigned procedure, the laparoscope was inserted, the tube was grasped with a biopsy forceps, coagulated and divided. The two cut ends were then re-coagulated. When the tubal rings were used, the ring applicator was inserted to permit the grasping forceps to pick up the isthmic portion of the tube, 2 to 3 cm from the corner of the uterus. A loop of the tube was drawn into the inner cylinder of the applicator, and the ring was applied to the loop by movement of the outer cylinder of the applicator.

After removing all instruments, the incision was closed with a nylon suture. The patient walked to the recovery room and after two to three hours returned home in the company of relatives. Prophylactic antibiotics were provided for five days for all patients.

Patients were asked to rate pain experienced during surgery as none, mild, moderate, severe, or very severe.

III. RESULTS

Women assigned the tubal ring technique were similar with respect to selected socio-demographic characteristics to those assigned the electrocoagulation techniques (Table I). There were no statistically significant differences.

Abnormal pelvic exams, usually cervical erosion, were reported for 28.7% of the tubal ring patients and 35.3% of the electrocoagulation patients. Pelvic infection was reported for 6.7% of the tubal ring patients compared with 10.0% of the electrocoagulation patients.

Technical Failures

Technical failure was defined as a case in which the assigned procedure could not be completed. Two patients who were assigned the ring technique had the procedure completed by electrocoagulation. In one case, the patient's mesosalpinx was torn by the ring applicator. The bleeding was stopped by electrocoagulation. The second patient had such a thick abdominal wall that the trocar was not long enough for the ring application. These patients are excluded from analysis of postsurgical complications and complaints because it would be impossible to decide to which technique to attribute the complications.

For two patients, the assigned technique of electrocoagulation, division, and recoagulation of the cut ends could be performed on only one tube because of edema or hydrosalpinx; the other tube was occluded by electrocoagulation alone.

Surgical Time

Surgical time was measured from the initial incision to final closure. Mean surgical time was 6.5 minutes for the tubal ring procedures, compared with a mean of 6.8 minutes for the electrocoagulation procedures. The difference was not statistically significant.

Surgical Difficulties, Complications, and Complaints

Surgical difficulties were defined as problems that occurred during the laparoscopic procedure. The rate of surgical difficulties was significantly higher ($p<.07$) for the tubal ring (12.0%) than for the electrocoagulation technique (6.0%), primarily as a result of the fogging of the lens of the laparoscope used during the tubal ring procedures (Table II). Adhesions caused the most frequent difficulty in the electrocoagulation cases.

Rates of surgical complications were similar for the tubal ring and electrocoagulation procedures. Ring complications included one case in which the mesosalpinx was torn by the ring applicator, causing a change in the technique of tubal occlusion; the second case involved a tear in the broad ligament by the ring applicator, but no bleeding occurred. The three electrocoagulation complications were oozing from the tube which required additional electrocoagulation.

The severity of pain reported by patients during the sterilization was significantly higher ($p<.001$) for the tubal ring procedures (Table III). Twice as many of the ring patients reported moderate or severe pain than did electrocoagulation patients.

Postoperative Complications and Complaints

Complications and complaints were grouped by the time of occurrence: during the recovery period, within 7 to 21 days after discharge from the hospital, or at 6 and 12 months after sterilization. A much higher ($p<.001$) proportion of the women who were sterilized with the tubal ring (52.7%) complained of pelvic/abdominal pain in the recovery period, as compared with those sterilized

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by electrocoagulation (16.0%) (Table IV). Complaints of pelvic/abdominal pain immediately after hospital discharge, however, were similar for the two groups.

Six-month follow-up was completed for all of the tubal ring and electrocoagulation patients. No pregnancies had occurred and no gynecological surgery was performed for patients in either group. Cervical erosion was reported for 29.7 percent of the ring and 30.9 percent of the electrocoagulation patients, figures similar to those found at the time of admission. About 48 percent of the tubal ring and 53 percent of the electrocoagulation patients complained of occasional pelvic and/or back pain at the time of the six-month follow-up.

Twelve-month follow-up was completed on 80 (54.1%) of the tubal ring and 80 (53.3%) of the electrocoagulation patients. No pregnancies or surgery were reported. Occasional, mild pelvic and back pain which did not require treatment was reported by 58 percent of the ring patients and 59 percent of the electrocoagulation patients. One suspected case of pelvic infection in the ring group was treated with antibiotics; no hospitalization was required.

IV. DISCUSSION

These results of the present analysis indicate that both tubal ring and standard electrocoagulation techniques of laparoscopic sterilization can be easily and safely performed with local anesthetics plus analgesics on an outpatient basis. Although the planned procedures could not be performed on two ring patients and two electrocoagulation patients, the ring technical failures presented more of a problem because a change to an alternate occlusion technique was required. For the two electrocoagulation cases, only a modification of the coagulation was required.

A higher rate of surgical difficulties, primarily lens fogging, was experienced with the tubal ring than with the electrocoagulation procedures. Replacement of the tubal ring laparoscope corrected this problem. A similar study has shown no differences in surgical difficulties[6].

Both techniques had clinically acceptable surgical complication rates. No serious complications such as bowel or bladder injuries occurred in this series. Tubal and mesosalpinx tears occurred with the ring applicator. Bleeding requiring recoagulation occurred with the electrocoagulation technique. Similar findings were reported in Korea[6].

No pregnancies were reported for either group, and the two techniques were equally free of adverse gynecological effects for the first year after surgery; no gynecological surgery was reported.

Pain during the procedure and in the immediate recovery period was more severe for patients sterilized by the tubal ring. Other studies report similar rates of pain during the recovery period [7-9] for women sterilized with mechanical devices; however, these reports also indicate that electrocoagulation patients experience the same[7-8] or more intense[9] pain than do patients sterilized by mechanical devices. By the time of the early follow-up visit, 7 to 21 days after surgery, ring and electrocoagulation patients reported similar rates of pelvic pain.

Despite the higher incidence of surgical difficulties and pain that is associated with the tubal ring, many physicians prefer the ring technique to electrocoagulation because it eliminates the possibility of inadvertent serious

electrical burns. There may also be a greater potential for reversibility, as less of the tube is damaged.

Improvements in the prototype tubal ring applicators may eliminate some of the surgical problems such as fogging of the lens and tearing of the tubes, just as improvements in bipolar electrocoagulation equipment may lessen the hazard of inadvertent electrical burns.

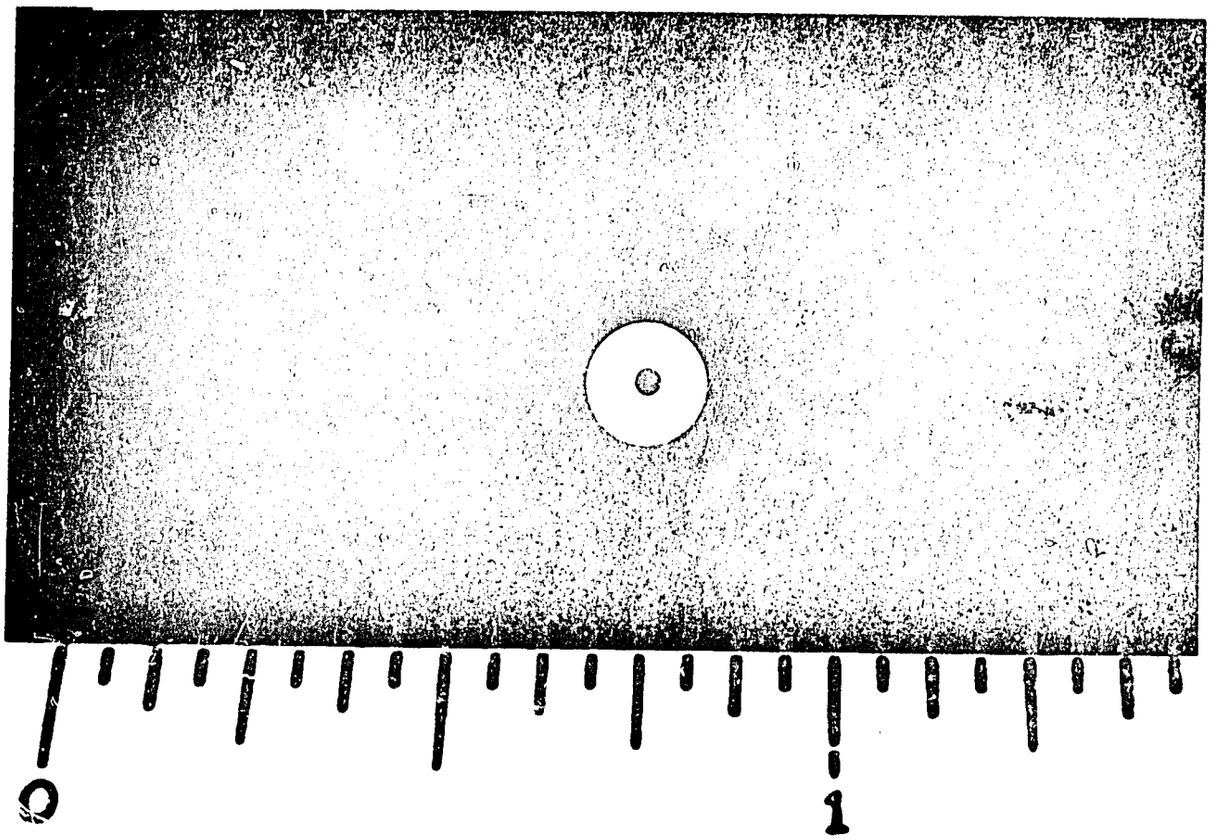

Figure 1. Tubal Ring.

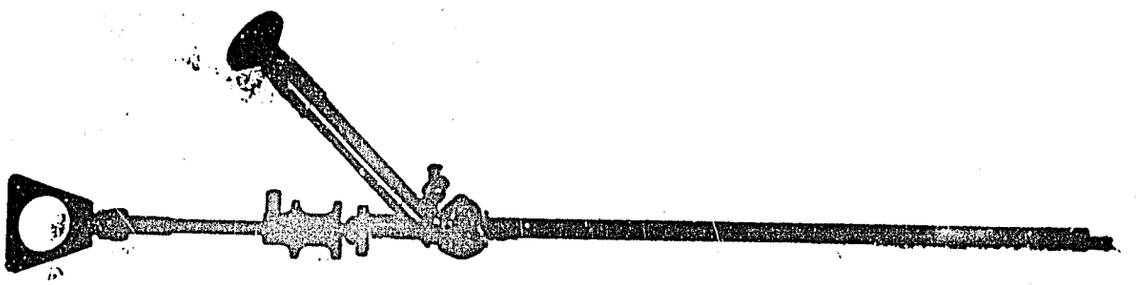

Figure 2. Tubal Ring Applicator. (Manufactured by KLI,Inc. 65 Industrial Drive, Ivyland, Pennsylvania 18974.)

Table I

SELECTED SOCIO-DEMOGRAPHIC CHARACTERISTICS OF WOMEN RANDOMLY ASSIGNED TO ELECTROCOAGULATION AND TUBAL RING TECHNIQUES OF LAPAROSCOPIC STERILIZATION IN THAILAND

	Electrocoagulation (N=150)		Tubal Ring (N=150)	
	No.	%	No.	%
Age (years)				
<30	61	40.6	60	40.0
30-34	40	26.7	52	34.7
35+	49	32.7	38	25.3
Mean	31.4		31.1	
Education (years)				
None	8	5.3	13	8.7
1-6	110	73.3	105	70.0
7-12	24	16.0	24	16.0
13+	8	5.3	8	5.3
Mean	5.2		4.9	
Parity				
2	48	32.0	44	29.3
3-4	71	47.4	77	51.4
5-6	25	16.6	24	16.0
7+	6	4.0	5	3.3
Mean	3.4		3.4	
Contraceptive Practice Prior to Sterilization				
None	10	6.7	5	3.3
Conventional	13	8.7	13	8.7
IUD	23	15.3	22	14.7
Orals	88	58.6	102	68.0
Other	16	10.7	8	5.3

Table II

SURGICAL DIFFICULTIES AND COMPLICATIONS BY PLANNED TECHNIQUES OF STERILIZATION

Difficulties	Electrocoagulation (N=150)		Tubal Ring (N=148)	
	No.	%	No.	%
Adhesions	8	5.3	3	2.0
Fogged lens	0	0.0	13	8.7
Patient movement	1	0.7	0	0.0
Edema of tubes	1	0.7	0	0.0
Hydrosalpinx	1	0.7	0	0.0
Thick abdominal wall	0	0.0	1	0.7
Procedures with one or more surgical difficulties	9	6.0	18	12.0
Complications				
Vomiting	1	0.7	0	0.0
Bleeding from Mesosalpinx, broad ligament or tube	3	2.0	2	1.4
Women with one or more surgical complications	4	2.7	2	1.3

Table III

DEGREE OF PAIN REPORTED BY PATIENTS
DURING STERILIZATION PROCEDURE

Degree of Pain	Electrocoagulation (N=150) No.	%	Tubal Ring (N=148) No.	%
None	5	3.3	16	10.8
Mild	114	76.0	71	48.0
Moderate	27	18.0	53	35.8
Severe	4	2.7	8	5.4

Table IV

PATIENT COMPLICATIONS AND COMPLAINTS
BY PERFORMED STERILIZATION TECHNIQUES

Complications/Complaints During the Recovery Period	Electrocoagulation (N=150)		Tubal Ring (N=148)	
	No.	%	No.	%
Pelvic and/or abdominal pain	24	16.0	78	52.7
Backache	9	6.0	16	10.8
Nausea, vomiting	1	0.7	1	0.7
General body pain	2	1.3	4	2.7
Women with one or more complications	0	0.0	0	0.0
Women with one or more complaints	36	24.0	99	66.9
Complications/Complaints Immediately After Hospital Discharge				
Fever treated with antibiotics	1	0.7	1	0.7
Pelvic and/or abdominal pain	41	27.3	45	30.4
Backache	16	10.7	17	11.5
Distended abdomen	10	6.7	7	4.7
General body pain	1	0.7	3	2.0
Women with one or more complications	1	0.7	1	0.7
Women with one or more complaints	68	45.3	72	48.6

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INTERNATIONAL EXPERIENCE WITH TUBAL STERILIZATION BY MINILAPAROTOMY

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I. INTRODUCTION

The practice of minilap sterilization is not new. The experience with the immediate paraumbilical postpartum minilap sterilization is vast. The advantages of making it part of the delivery experience, without affecting the postpartum course, the few contraindications, the minimal morbidity, the high success rate, and the convenience for the patient are well documented.

More recently, interval suprapubic minilap sterilization is becoming a procedure of choice. The success rates of this technique are excellent. It is as simple to perform as its forerunner, requiring minimal surgical instrumentation and anesthesia. Consequently, both operating time and hospitalization are short, and the cost of care is modest. The experiences of Dr. Vitoon, a designer of the approach, and the literature testify to the mounting acceptance of this method, not only in developing countries, but in industrialized societies as well.

Ideally, comparative studies of minilap vs. other sterilization techniques should be conducted within the same institution, preferably by the same surgeon, under the same conditions. Such an assessment is currently under way in an international collaborative effort among the participants of the study, as well as other centers, under the aegis of the International Fertility Research Program (IFRP). Consistent with the enunciated purpose of this organization is its effort to identify new methods of fertility regulation, particularly where implications for reaching broad-based segments of a population are demonstrable.

IFRP staff have been actively involved in analyzing and evaluating female sterilization studies in many parts of the world. This presentation focuses on the IFRP international experience with 2820 tubal sterilizations performed in 11 countries at 19 collaborating centers by the minilaparotomy approach.

MATERIALS AND METHODS

Subjects

The patients were self-selected. They were women who came to the clinic/hospital requesting sterilization. Their mean age was 31.2 years and they were of high parity. Table II represents the socio-demographic characteristics of sterilized patients. It is interesting to note that about 42 percent were not using any form of contraception prior to undergoing the sterilization procedure.

Techniques

Although all techniques were performed through a suprapubic incision, there were variations in premedication given, anesthesia administered, and the means of manipulating the uterus, localizing and grasping the tubes, and occluding the tubes. Step-by-step technique descriptions have been provided by each contributer. Table I presents the distribution of minilap cases by the type of procedure and the technique of tubal occlusion.

A procedure was classified as a uterine elevation procedure if a uterine manipulator and no additional equipment for abdominal retraction was used. Manipulators used included Vitoon's manipulator (slide), Hulka's controlling tenaculum ( ), a Rubin cannula ( ) and a uterine sound traversing a Foley catheter ( ).

In both the proctoscopic or abdominal retractor categories, some sort of instrument was used for retracting the abdominal incision as a means of visualizing the tubes. This was done regardless of whether a uterine manipulator was used ( ).

If none of this equipment was used, the procedure was classified as digital manipulation.

The "other" category covers a range of techniques. They include: "minilap laparoscopy", which involves the use of the laparoscopic optics through a suprapubic minilap incision for visualizing and grasping the tubes, followed by a Pomeroy or a tubal ring occlusion ( ); and the Vacu-Lap technique where the tube is grasped by a small suction cup through a cylinder and then a Pomeroy is performed through a sliding window ( ).

Another variation is El-Kadi's technique, a combined suprapubic modified Pomeroy or tubal band application under laparoscopic guidance inserted paraumbilically ( ). There were also a few cases sterilized through an umbilical hernia incision.

Means of tubal occlusion included primarily the classic Pomeroy/Madlener, Kroner type fimbriectomy ( ), salpingectomy, and the application of the newly developed tubal rings ( ). The majority of the patients (93%) were sterilized by the Pomeroy (79%) or the tubal ring (14%) techniques.

Type of Anesthesia

Analgesia, combined with local anesthetic was administered in 55.3% of the cases, while 15.4% required general anesthesia, as shown in Table III.

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III. RESULTS

Surgical Time

The average surgical time was 20 minutes, as shown in Table V.

Hospitalization Time

One fourth of the patients were discharged the same day of surgery. Many of the patients who remained overnight did so for personal reasons rather than out of medical necessity. Data are presented in Table VIII.

Surgical Difficulties

Varying degrees of surgical difficulties were encountered in about 10 percent of the procedures, but there were no surgical failures forcing the abandonment of the sterilization. However, in 5 cases, it was possible to occlude only one tube. A number of surgical difficulties are delineated in Table IV. They include problems in reaching the peritoneum, interference of the bowel or omentum, and exteriorizing the tubes, especially in the presence of adhesions or retroverted uteri. Obesity and inadequate analgesia or anesthesia could be inhibiting factors.

Surgical Complications

Table VI shows complications encountered at the time of surgery. The rate (0.6%) of surgical complication was very low, and included primarily tubal tears, bladder/bowel injuries, uterine perforations, and blood loss in excess of 100 ccs.

In the immediate postoperative period and prior to discharging the patient from the hospital, complication rates again were minimal (less than 1%) as shown in Table VIII.

However, 22.7 percent of the women experienced one or more minor side effects, mainly wound or abdominal pain.

Postoperative Follow-up of Patients

Table XI represents the early postoperative follow-up within 7-21 days of the sterilization procedure. As noted, only 5.1 percent of the patients experienced one or more complications, including primarily fever and wound problems. On the other hand, 21.8 percent of the patients experienced manageable sequelae in the form of wound problems, pelvic pain, spotting and gastrointestinal discomfort (Table XII). These data appear to reinforce the assumptions made concerning the safety of this type of intervention.

There are six-month follow-up data available for only 741 of the 2820 patients, and one year follow-up data for very few patients. The over-all six-month pregnancy rate is 0.4 percent. It should be noted that all of the failures were on cases sterilized by the Pomeroy technique. No failures have yet been recorded for the tubal ring group.

Discussion

The experience of IFRP international contributors indicates that the mini-lap approach for interval female sterilization can be performed safely. There were no deaths reported during the surgical procedure, immediately postoperative, nor up to the time of the 7- to 21-day follow-up. The procedures used were simple. For the most part, they did not require expensive equipment, nor was it necessary to resort to general anesthetic except in certain cases where cultural patterns and patients' demands prevailed.

Surgical difficulties were encountered in about 10 percent of the cases; all were manageable, requiring only average surgical skill. While this reflects the simplicity and safety of the minlap procedure, it must not preclude training programs in endoscopy, especially in teaching institutions where the application of endoscopic procedures goes far beyond sterilization requirements.

Surgical complications were encountered in 1.6 percent of the patients and included bladder/bowel injury and uterine perforation. These rates, though small, were somewhat higher than the rates reported in a similar analysis of international IFRP pooled laparoscopy studies (0.2%). However, when the rate of bleeding of the tubes in the minilap and laparoscopy series were reviewed, it was found to be 0.9 percent in both groups.

In the 7- to 21-day follow-up of the minilap patients, fever or wound infection accounted for the high rate of complications (5.1%) compared to the rate of 1.4 percent for IFRP laparoscopy cases.

In both approaches, such complications are in accordance with what is reported in the literature ( ). They can be reduced to a minimum and are even preventable by careful screening of patients requesting sterilization, by the choice of a suitable sterilization technique, mandatory emptying of the bladder, and testing for uterine mobility.

Here again, the comparability of international pooled data of minilap versus laparoscopy should be interpreted with caution. It is not merely that cases were sterilized by physicians with varying degrees of training and experience. The levels of medical care in their individual institutions, the dissimilar environmental conditions, the adherence to rigid aseptic surgical

techniques, and the health status and cultural patterns of their patients must all be taken into account.

Conclusion

The IFRP recognizes that the ideal sterilization procedure has yet to be evolved. The organization is continuing to monitor research in innovative techniques and approaches to tubal occlusion and to encourage efforts to make the process as safe, as reliable, as inexpensive, and even as reversible as possible. It would appear that minilaparotomy presents a useful alternative.

The author wishes to sincerely acknowledge the enormous effort, especially, of Linda Lewis and Margaret McCann, and the staff of the IFRP in providing the data for this presentation.

EARLY POSTOPERATIVE COMPLAINTS
POOLED IFRP STUDIES
(N = 2686)*

Complaint	No.	%
Vaginal hair itchiness	198	7.4
Pelvic pain	142	5.3
General shoulder pain	84	3.1
Vaginal bleeding	37	1.4
Gastrointestinal problems	31	1.2
Syncope dizziness	20	0.7
Headache	16	0.6
Backache	13	0.5
Dysuria	12	0.4
Other	32	1.1
Women with one or more early postoperative complaints	**585**	**21.8**

* *134 patients (4.8%) were not observed at the 7–21 day follow-up visit.*

EARLY POSTOPERATIVE COMPLICATIONS
POOLED IFRP STUDIES
(N = 2686)*

Complication	No.	%
Fever		
Requiring antibiotics	71	2.6
Not requiring antibiotics	2	0.1
Wound infection	70	2.6
Urinary tract infection	6	0.2
Hematoma of abdominal wall	1	0.1
Subacute salpingitis	1	0.1
Women with one or more early postoperative complications	**136**	**5.1**

* *134 patients (4.8%) were not observed at the 7–21 day follow-up visit.*

SURGICAL COMPLICATIONS
POOLED IFRP STUDIES
(N = 2820)

Complication	No.	%
Tube torn/bleeding	25	0.9
Bowel/bladder injury	8	0.3
Uterine perforation	7	0.2
Excessive blood loss (>100 ml)	5	0.2
Ovarian laceration	2	0.1
Cervical laceration	2	0.1
Women with one or more surgical complications	44	1.6

DURATION OF HOSPITALIZATION AFTER SURGERY
POOLED IFRP STUDIES
(N = 2817)*

Nights Hospitalized	No.	%
0	647	23.0
1–2	1922	68.2
3–4	133	4.7
5–6	30	1.1
7+	85	3.0
MEAN**	2.0	

* *Data missing for three cases*

** *Mean number of nights' hospitalization of patients hospitalized one or more nights.*

DIFFICULTIES AT SURGERY
POOLED IFRP STUDIES
(N = 2820)

Number of procedures 287

Percentage of procedures 10.2

MAJOR SURGICAL DIFFICULTIES
POOLED IFRP STUDIES
(N = 2820)

Difficulty	No.	%
Bowel bladder/omentum interference	70	2.5
Adhesions	59	2.1
Difficulty opening peritoneum	40	1.4
Difficulty ligating tubes	27	1.0

OTHER DIFFICULTIES AT SURGERY
POOLED IFRP STUDIES
(N = 2320)

Difficulty	No.	%
Obesity	17	0.6
Difficulty visualizing/exteriorizing tubes	15	0.5
Retroverted uterus	14	0.5
Movement of patient	14	0.5
Inadequate analgesia/anesthesia	10	0.4
Difficulty manipulating uterus	8	0.3
Ovarian cyst	8	0.3
Difficulty closing peritoneum	5	0.2

Women with one or more surgical complications

SURGICAL TIME
POOLED STUDIES
(N = 2820)

Surgical Time (Minutes)	No.	%
Less than 10	259	9.2
10–19	1425	50.5
20–29	642	22.8
30–39	295	10.5
40 or more	199	7.1
Mean	**19.6**	

TYPE OF ANESTHETIC ADMINISTERED
POOLED IFRP STUDIES
(N = 2820)

Anesthetic	No.	%
Local, with analgesics	1560	55.3
Local only	549	19.5
General	433	15.4
Regional	232	8.2
Other/unknown	46	1.6

TYPE OF MINILAP PROCEDURE AND TECHNIQUE OF TUBAL OCCLUSION POOLED IFRP STUDIES

Minilap Procedure	Pomeroy/ Madlener *(N = 2215)*	Fimbriectomy/ Salpingectomy *(N = 126)*	Tubal Ring *(N 409)*
Uterine elevation *(N = 1405)*	1179	22	204
Proctoscopic *(N = 172)*	90	80	2
Abdominal retraction *(N = 258)*	59	0	199
Digital manipulation *(N = 899)*	875	24	0
Other *(N = 86)*	12	0	4
Total *(N = 2820)*	2215	126	409

* *Other techniques were used in 70 cases.*

SELECTED SOCIO-DEMOGRAPHIC CHARACTERISTICS
POOLED IFRP STUDIES
(N = 2820)

Mean age (years)	31.2
Mean parity	5.2
Mean number of living children	4.8
Mean age of youngest child (years)	2.5
Mean patient's education (completed years)	4.6
Mean husband's education (completed years)	5.0
Percent using contraception before sterilization	58.1

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FEMALE STERILIZATION
SERIES NO. 81

INTERNATIONAL FERTILITY RESEARCH PROGRAM
CONFERENCE PAPER

LAPAROSCOPY VERSUS COLPOTOMY: A REPORT FROM COLOMBO, SRI LANKA

By
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Presented at
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Bangkok, Thailand
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LAPAROSCOPY VERSUS COLPOTOMY: A REPORT FROM COLOMBO, SRI LANKA

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LAPAROSCOPY VS. COLPOTOMY: A REPORT FROM COLOMBO, SRI LANKA

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The laparoscopy sterilization procedure has been associated with possible risk of electrical injury, particularly to the bowel; the colpotomy procedure has had high incidences of infection and hemorrhage. This limited series of laparoscopy and colpotomy represent the initial learning experience of the operator with these methods of sterilization. This report analyzes 106 procedures of fimbriectomy via colpotomy and 143 procedures of electrocoagulation via laparoscopy performed on women who had not recently been pregnant. Two laparoscopy procedures and one colpotomy procedure were considered to be technical failures because the procedures were not completed as planned. Surgical complications included eight (5.6%) cases of minor patient electrical shock resulting from problems with the cautery equipment and seven (6.6%) cases of bleeding from the colpotomy incision. At the 7- to 21-day follow-up examination colpotomy patients had a higher incidence of fever treated with antibiotics (9.4%) than did laparoscopy patients (.7%). Major complications requiring hospital readmission occurred only for colpotomy patients. The mechanical, technical, and clinical problems that occurred in this series exemplify those which can occur with the introduction of any new procedure or technology.

I. INTRODUCTION

Two methods of interval female sterilization--electrocoagulation through laparoscopy and fimbriectomy through posterior colpotomy--were introduced at the De Soysa Hospital for Women in Colombo, Sri Lanka in late 1973. Although most sterilizations during this period were still being performed during the hospitalization for childbirth, the demand for interval sterilization was increasing.

Laparoscopy and colpotomy are both procedures that can be readily performed for women who have not recently been pregnant (1-4). Hospitalization time is short--the patient can often be discharged on the day of surgery. Both procedures are highly complex, however, and require special training. While both laparoscopy and colpotomy are medically acceptable procedures, several factors will determine the suitability of the procedure in the specific clinical settings. Patient acceptability of both procedures may vary; some patients prefer colpotomy because of the absence of a visible scar, while others prefer laparoscopy because it is not followed by an abstinance from sexual intercourse suggested for vaginal procedures.

Patient characteristics influence the choice of procedure. For example, previous extensive abdominal surgery, which can lead to abdominal and upper pelvic adhesions, may make colpotomy the more suitable procedure.

Laparoscopic equipment is complex and expensive and requires meticulous care and maintenance, while colpotomy can be performed with simple, inexpensive instruments that are usually available wherever gynecological services are offered.

Complication rates can be acceptably low for both procedures, but may vary depending on such factors as the technique of tubal occlusion and the expertise and experience of the surgeon. There is an absence of comparable data on complication rates of laparoscopy and colpotomy, but is is generally believed that the rate of complications following colpotomy is higher than that following laparoscopy (5).

This study compares the safety, effectiveness, and ease of performance of laparoscopy and posterior colpotomy sterilization.

I. MATERIALS AND METHODS

From June 1974 through January 1976, 249 women were sterilized at the De Soysa Hospital for Women in Colombo, Sri Lanka. Data on 143 patients selected as suitable for laparoscopy and 106 patients selected as suitable for colpotomy were recorded on standard forms designed to obtain information from the time of surgery to 12 months after sterilization.

Study Design

All sterilizations were performed at the same institutions during the same time period and one operator performed all surgical procedures; thus, the data on the two procedures are comparable. Only those women requesting sterilization for family planning purposes who had not recently been pregnant were included in the study. Patients were scheduled for 3 follow-up visits after surgery: at 7-to-21 days, 6 months, and 12 months.

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Analysis

All statistical tests were performed using a significance level (p. value) of 0.05.

Sterilization Procedures

Prior to sterilization, routine physical and pelvic examinations and urinalysis and hematocrit tests were performed for each patient.

For laparoscopy, the patient was admitted the night before surgery or on the morning of surgery. The patient was told not to eat breakfast, but no enema was given. A preoperative medication of 50 mg of meperidine and 0.6 mg of atropine was given one half hour before surgery. The procedure was performed under general anesthesia. The laparoscopy procedure used was the double puncture technique described by Dr. Raoul Palmer (6,7). Each tube was identified, grasped with the Palmer electrocoagulation forceps 2 cm from the uterine cornu, then coagulated and divided. After she rested for four to six hours, the patient was discharged. No dietary or activity restrictions were necessary.

For posterior colpotomy, the patient was admitted the night before surgery. An enema was given the morning of surgery. The procedure was initially performed under low spinal anesthesia, but this was discontinued in the latter part of the series because of the high incidence of postoperative headaches and backaches. General anesthesia was used in the later procedures. The vaginal procedure used was that described by Dr. Rustom Soonawala (8). In an effort to reduce the possibility of infection, the operation was performed, where possible, without any contact with the pelvic viscera. The peritoneum and vaginal mucosa were closed in one layer after any bleeding points had been ligated. Patients given spinal anesthesia remained in the hospital overnight; general anesthesia patients

often were discharged a few hours after surgery. Patients were advised against coitus for four weeks.

III. RESULTS

Subjects

Women undergoing laparoscopy were similar with respect to selected socio-demographic characteristics to those undergoing posterior colpotomy (Table I).

Technical Failures

Technical failure was defined as a case in which the planned procedure could not be completed. For two (1.4%) of the laparoscopy patients, the planned technique could not be completed. In one case, the right tube was adhered to the omentum and bowel, preventing occlusion by electrocoagulation. Laparotomy was performed and the tube was occluded by ligation. The second patient had adhesions around the right tube and the omentum that prevented visualization of the tube; no procedure was performed on that tube.

For one (0.9%) colpotomy patient, the planned technique could not be completed; the left tube was occluded by fimbriectomy, but the right tube was occluded by the Pomeroy technique because exposure of the right fimbria was difficult.

Anesthesia Complications and Complaints

General anesthesia was used for all the laparoscopy procedures; for colpotomy procedures, regional anesthesia (spinal) was used for 62.2 percent, general anesthesia for 36.8 percent, and local anesthesia for 1.0 percent.

Rates of anesthesia-related complications and complaints were similar for the laparoscopy and colpotomy procedures (Table II). Vomiting was the most frequently reported complication for both laparoscopy (4.9%) and colpotomy (4.7%) patients. Hoarseness was the most frequently reported complaint for laparoscopy patients (11.2%), and headaches were reported most frequently for colpotomy patients (21.7%); all the colpotomy patients reporting headache had received regional anesthesia.

Surgical Difficulties and Complications

Surgical difficulties were defined as problems that occurred during the sterilization procedure. The rate of surgical difficulties was significantly higher for the laparoscopy (46.9%) than for the colpotomy (20.8%) procedures (Table III). The most frequent problem in both procedures (in 29.4% of laparoscopy and 15.1% of colpotomy procedures) was difficulty visualizing or exteriorizing the tubes. During laparoscopy the intestines frequently interfered with visualization, but were easily displaced with an interperitoneal probe, making this a minor difficulty. Another source of difficulties during laparoscopy was equipment problems (14.0%), including gas leakage, inadequate insulation, and lens fogging.

Rates of surgical complications were similar for the laparoscopy (9.8%) and colpotomy (7.5%) procedures. Most of the laparoscopy complications resulted from equipment problems: eight patients (5.6%) experienced mild electrical shock through the Palmer electrocoagulation forceps. Contact between the metal of the forceps (exposed because of inadequate insulation) and the metal of the trocar sleeve produced a mild electrical shock to both the patient and the operator. Until the forceps could be replaced with a completely insulated model, conscious effort was made to ensure that only the insulated area on the forceps came in

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TABLE I

SELECTED SOCIO-DEMOGRAPHIC CHARACTERISTICS OF WOMEN UNDERGOING LAPAROSCOPY AND COLPOTOMY STERILIZATION

	Laparoscopy Electro-coagulation *(N = 143)*		Colpotomy Fimbriectomy *(N = 106)*	
	No.	%	No.	%
Age (years)				
< 30	59	41.2	44	41.6
30-34	38	26.6	33	31.1
35+	46	32.2	29	27.3
Mean	31.3		31.3	
Education (years)				
None	5	3.5	4	3.8
1–6	53	37.1	33	31.1
7–12	83	58.0	68	64.2
13+	2	1.4	1	0.9
Mean	7.2		7.2	
Parity				
1–2	41	28.7	21	19.8
3–4	69	48.2	55	51.9
5–6	23	16.1	22	20.8
7+	10	7.0	8	7.5
Mean	3.6		4.0	
Contraceptive practice prior to sterilization				
None	46	32.1	39	36.8
Conventional	32	22.4	15	14.1
IUD	34	23.8	35	33.0
Orals	22	15.4	13	12.3
Other	9	6.3	4	3.8

TABLE II

ANESTHESIA COMPLICATIONS AND COMPLAINTS OF WOMEN UNDERGOING LAPAROSCOPY AND COLPOTOMY STERILIZATION

	Laparoscopy Electro-coagulation *(N = 143)*		Colpotomy Fimbriectomy *(N = 106)*	
	No.	%	No.	%
Anesthesia complications				
Vomiting	7	4.9	5	4.7
Shock	0	0.0	1	0.9
Hypotension	0	0.0	1	0.9
Aspiration	1	0.7	0	0.0
Bronchospasm	1	0.7	0	0.0
Women with one or more anesthesia complications	9	6.3	7	6.6
Anesthesia complaints				
Headache	5	3.5	23	21.7
Hoarseness	16	11.2	0	0.0
Giddiness	6	4.2	0	0.0
Nausea	4	2.8	0	0.0
Muscle pain/backache	1	0.7	3	2.8
Women with one or more anesthesia complaints	25	17.5	26	24.5

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TABLE III

SURGICAL DIFFICULTIES AND COMPLICATIONS OF WOMEN UNDERGOING LAPAROSCOPY AND COLPOTOMY STERILIZATION

	Laparoscopy Electro-coagulation *(N = 143)*		Colpotomy Fimbriectomy *(N = 106)*	
	No.	%	No.	%
Surgical difficulties				
Equipment problems				
Leakage of gas, through forceps	19	13.3	–	–
Lens fogging	1	0.7	–	–
Adhesions	4	2.8	2	1.9
Difficulty visualizing or exteriorizing tubes	42	29.4	16	15.1
Difficulty entering peritoneal cavity	0	0.0	3	2.8
Difficulty inducing pneumoperitoneum	1	0.7	–	–
Movement of patient	1	0.7	0	0.0
Hydrosalpinx	0	0.0	1	0.9
Procedures with one or more surgical difficulties	67	46.9	22	20.8
Surgical complications				
Mild electrical shock from equipment	8	5.6	–	–
Extraperitoneal insufflation of gas	3	2.1	–	–
Hematoma of mesosalpinx/tube	2	1.4	0	0.0
Bleeding from incision	0	0.0	7	6.6
Bleeding from tube requiring recautery	1	0.7	–	–
Shock	0	0.0	1	0.9
Transfusion	0	0.0	1	0.9
Women with one or more surgical complications	14	9.8	8	7.5

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contact with the sleeve. The most frequently reported surgical complication for the colpotomy procedures was bleeding from the edges of the incision (6.6%); bleeding points were ligated before closing the incision.

Postoperative Complications and Complaints

Complications and complaints were analyzed by the time of occurrence: during the recovery period before discharge, within 7 to 21 days after discharge from the hospital, or at 6 and 12 months after sterilization. None of the laparoscopy patients reported complications during the immediate recovery period, compared with three (2.9%) of the colpotomy patients (Table IV). Laparoscopy patients had a higher rate of complaints (32.6%) than colpotomy patients (21.9%), but the difference was not statistically different. In both groups of patients, abdominal or pelvic pain was the most frequent complaint.

A much higher proportion of the women who were sterilized by colpotomy (17.2%) reported complications at the 7- to 21-day follow-up visit, compared with those sterilized by laparoscopy (5.0%) (Table V). Fever treated with antibiotics (9.5%) and vaginal bleeding (7.6%) were the two most frequent complications reported by colpotomy patients. Rates of complaints reported at this visit were also significantly higher for colpotomy patients (13.2%), as compared with laparoscopy patients (5.7%).

Six-month follow-up was completed for all of the laparoscopy and colpotomy patients. The six-month complication rate was significantly higher for colpotomy patients (23.8%) than for laparoscopy patients (3.6%) (Table VI). Incision complications, vaginitis, and pelvic/urinary infection contributed to the higher rate. The rate of reported complaints for colpotomy patients was also significantly higher.

TABLE IV

RECOVERY PERIOD COMPLICATIONS AND COMPLAINTS OF WOMEN UNDERGOING LAPAROSCOPY AND COLPOTOMY STERILIZATION

	Laparoscopy Electro-coagulation *(N = 141)*		Colpotomy Fimbriectomy *(N = 105)*	
	No.	%	No.	%
Recovery period complications				
Fever, treated with antibiotics	0	0.0	1	1.0
Vaginal discharge	0	0.0	1	1.0
Vomiting	0	0.0	1	1.0
Diarrhea	0	0.0	1	1.0
Women with one or more complications	**0**	**0.0**	**3**	**2.9**
Recovery period complaints				
Shoulder/chest pain	19	13.5	4	3.8
Abdominal/pelvic pain	24	17.0	16	15.2
Back pain	2	1.4	2	1.9
General body pain	0	0.0	1	1.0
Dizziness	1	0.7	0	0.0
Women with one or more complaints	**46**	**32.6**	**23**	**21.9**

TABLE V

EARLY FOLLOW-UP COMPLICATIONS AND COMPLAINTS OF WOMEN UNDERGOING LAPAROSCOPY AND COLPOTOMY STERILIZATION

	Laparoscopy Electro-coagulation *(N = 141)*		Colpotomy Fimbriectomy *(N = 105)*	
	No.	%	No.	%
Follow-up complications				
Fever				
Treated with antibiotics	1	0.7	10	9.5
Not treated with antibiotics	1	0.7	0	0.0
Vaginal bleeding	0	0.0	8	7.6
Vaginal discharge	0	0.0	2	1.9
Incision complications				
Delayed healing	2	1.4	0	0.0
Infection	3	2.1	0	0.0
Pelvic infection	0	0.0	1	1.0
Women with one or more complications	**7**	**5.0**	**18**	**17.2**
Follow-up complaints				
Dysuria	2	1.4	2	1.9
Pain during defecation	0	0.0	2	1.9
Back pain	1	0.7	6	5.7
Abdominal/pelvic pain	2	1.4	3	2.9
Shoulder/chest pain	2	1.4	2	1.9
Nausea	1	0.7	0	0.0
Dizziness	0	0.0	1	1.0
Women with one or more complaints	**8**	**5.7**	**16**	**13.2**

TABLE VI

LATE FOLLOW-UP COMPLICATIONS AND COMPLAINTS OF WOMEN UNDERGOING LAPAROSCOPY AND COLPOTOMY STERILIZATION

	6–month				12–month			
	Laparoscopy Electro-coagulation *(N = 141)*		Colpotomy Fimbriectomy *(N = 105)*		Laparoscopy Electro-coagulation *(N = 104)*		Colpotomy Fimbriectomy *(N = 74)*	
	No.	%	No.	%	No.	%	No.	%
Long-term complications								
Incision complications								
Drainage	0	0.0	1	1.0	0	0.0	0	0.0
Suture problems (granulated tissue)	0	0.0	10	9.5	0	0.0	2	2.7
Separation	0	0.0	2	1.9	0	0.0	0	0.0
Infection	1	0.7	0	0.0	0	0.0	0	0.0
Vaginitis, vaginal discharge	2	1.4	10	9.5	2	1.9	3	4.1
Dysfunctional bleeding	1	0.7	0	0.0	5	4.8	2	2.7
Pelvic, urinary infection	0	0.0	3	2.9	1	1.0	1	1.4
Hemorrhage	0	0.0	2	1.9	0	0.0	1	1.4
Amenorrhea	0	0.0	0	0.0	0	0.0	1	1.4
Women with one or more complications	5	3.6	25	23.8	8	7.7	10	13.5
Long-term complaints								
Dysuria	1	0.7	0	0.0	0	0.0	1	1.4
Pelvic/back pain, related to surgery	4	2.8	17	16.2	2	1.9	5	6.8
Incision pain	0	0.0	2	1.9	1	1.0	0	0.0
Women with one or more complaints	5	3.5	19	18.1	3	2.9	6	8.2

Twelve-month follow-up was completed for 105 (73.8%) of the laparoscopy patients and 74 (70.5%) of the colpotomy patients. Twelve-month complication rates were similar for the two procedures; the complication rate had increased for the laparoscopy patients (7.7%) and decreased for the colpotomy patients (13.5%) (Table VI). Rates of reported complaints were also similar for the two procedures.

Three of the colpotomy patients were readmitted to the hospital between the time of discharge and the 7- to 21-day follow-up visit. One patient was admitted for treatment of pelvic infection that had been present and treated with antibiotics at the time of surgery. A second patient was admitted for vaginal bleeding, and the third was treated for dysuria and vaginal discharge.

Three other colpotomy patients were readmitted to the hospital between the 7- to 21-day follow-up visit and the six-month follow-up. Two were admitted for bleeding from the vaginal cuff; bed rest was the prescribed treatment in one case, but the second case required a blood transfusion and packing of the vagina. The third patient was admitted for pelvic infection that was treated with and responded to antibiotics.

There were no readmissions for the laparoscopy patients.

Pregnancies

One woman was pregnant at the time of sterilization and thus her pregnancy was not the result of a method failure. Two other pregnancies occurred subsequent to sterilization in the laparoscopy group. One of these occurred four months after surgery, an electrocoagulation failure. The second occurred in one of the technical failure cases 11 months after surgery; an ectopic pregnancy was

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found on the side where the tube was occluded by the Pomeroy technique through a laparotomy.

No pregnancies were reported among the patients sterilized by colpotomy.

Hospitalization

The number of nights of hospitalization after sterilization was higher for colpotomy patients because most had been given spinal anesthesia. Almost 60.0 percent of the laparoscopy patients were discharged the day of surgery, compared with less than 20.0 percent of the colpotomy patients. For those patients remaining in the hosptial after surgery, mean hospitalization time was similar for the two procedures (1.3 and 1.2 nights for laparoscopy and colpotomy patients, respectively).

IV. DISCUSSION

The present analysis shows some of the advantages and disadvantages of laparoscopy and colpotomy procedures for interval female sterilization.

Laparoscopy had a significantly higher rate of surgical difficulties than did colpotomy, but surgical complication rates were similar for both procedures. Although many of the laparoscopic surgical difficulties were minor, the laparoscopy procedures were plagued with equipment problems that included lens fogging, leakage of gas, and lack of adequate forceps insulation. These problems not only increased difficulty in performing the procedures in some cases, but they also resulted in complications. Equipment problems have often been associated with electrocoagulation via laparoscopy (1,2) and are potential problems

with any highly complex and technical piece of equipment. The colpotomy surgical difficulties and complications were similar to those found in other studies of vaginal ligation: difficulty in visualizing and/or exteriorizing the tubes and bleeding from the incision (3,4).

Complications reported during the recovery period before discharge, at the 7- to 21-day follow-up visit, and at the six-month follow-up visit were much higher for the colpotomy patients. Twelve-month rates were similar for the two methods.

Five colpotomy patients were readmitted to the hospital for bleeding and infection complications related to sterilization: another was admitted for treatment of pelvic infection that had been present at the time of surgery. This corresponds to findings in at least one other colpotomy study with long-term follow-up (9). Major complications requiring hospital readmission occurred only for colpotomy patients; none of the laparoscopy patients were readmitted because of complications.

Two of the laparoscopy patients became pregnant after sterilization, one of whom had her tubes occluded by electrocoagulation and one of whom underwent laparotomy with tubal occlusion by ligation because of adhesions. No subsequent pregnancies were reported among patients sterilized by colpotomy.

This limited series of both laparoscopy and colpotomy sterilization procedures represents the initial learning experience of the operator with these methods of sterilization. New technologies offer potential improvements for the patient, but such improvements will not occur until the specialized training received by the physician is followed by adequate experience. The newness of

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these procedures to the De Soysa Hospital was evident in the results of the current series. General and spinal anesthesia were used, rather than local, until clinical expertise was developed. The mechanical, technical, and clinical problems that occurred exemplify those which can occur with the introduction of any new procedure and technology. With experience and resolution of equipment problems, great improvement has been seen in the clinical performance of interval female sterilization at the De Soysa Hospital in Colombo, Sri Lanka.

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LAPAROSCOPIC STERILIZATION WITH TUBAL RINGS

By

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Abstract

Laparoscopic Sterilization With Tubal Rings

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The use of tubal rings for tubal occlusion at laparoscopy was evaluated in 291 interval procedures performed at Kandang Kerbau Hospital, Singapore. The technique appears to be safe and effective based on the absence of major complications and on the low (1.0%) failure rate.

I. INTRODUCTION

The rising demand for contraceptive female sterilization services in Singapore may be attributed to the increased recognition among women of the need to limit family size and to the increased availability of sterilization procedures that can be performed on an outpatient basis. Providing safe and effective methods of sterilization is the key to the success of an extensive sterilization program such as the one in Singapore. Although laparoscopic sterilization procedures using electrocoagulation techniques for tubal occlusion have been demonstrated to be safe and effective, they are nevertheless associated with potentially serious complications including bowel injury and haemorrhage. In an effort to decrease the risk of complications associated with laparoscopic electrocoagulation procedures while still providing procedures associated with low rates of failure, several mechanical methods of tubal occlusion have been devised and evaluated for use at laparoscopy, including the tubal ring (1), spring-loaded clip (2), and snare techniques (3).

Since March 1975, the tubal ring has been used for elective female sterilization at Kandang Kerbau Hospital, Singapore. This report presents a summary of our initial experiences with the tubal ring in 291 single-incision laparoscopic procedures.

II. METHODS AND MATERIALS

From March 1975 to July 1976, 291 women who had not recently been pregnant underwent laparoscopic sterilization, with tubal rings used for tubal occlusion, at the Unit of the Senior Obstetrician and Gynaecologist, Kandang Kerbau Hospital.

Laparoscopic Procedures

All laparoscopic sterilization procedures were performed in a standard manner by one surgeon (D.V.). Since the laparoscopic procedure has been described in detail in numerous publications, only those aspects of the procedure which may be different from the norm and those aspects relating to the application of tubal rings are presented.

Patients were admitted to the hospital the night before the sterilization. All procedures were performed under local anesthesia. Five minutes before the start of the procedure, patients were premedicated with 10 mg diazepam and 50 mg meperidine administered intravenously. Pneumoperitoneum was achieved with about two liters of CO_2.

The laparoscope (Figure 1) used for the application of the tubal rings incorporates a standard laparoscopic lens system and a tubal ring applicator system consisting of two cylinders and a retractable grasping forceps for lifting and holding a segment of Fallopian tube. The tubal rings are 2.5 mm thick, with a 1 mm inner diameter and 4 mm outer diameter and are made of dimethylpolysioxane with 5 percent barium sulfate. A tubal ring is loaded onto the inner cylinder of the applicator (5.4 mm diameter) immediately before application to the Fallopian tube. When stretched to 6 mm, the tubal ring has a 100 percent memory rate.

Once the Fallopian tube is identified, it is grasped at its isthmic portion with the forceps and elevated. The forceps are retracted into the inner cylinder of the applicator, thus withdrawing a segment of the tube into the applicator. By withdrawing the inner cylinder further within the applicator, the tubal ring is pushed off the inner cylinder onto the grasped segment of the Fallopian tube contained within the inner cylinder. The forcep is moved forward to release the loop of Fallopian tube. The result is a Madlener-type of tubal occlusion (Figure 2). The laparoscope is withdrawn from the peritoneal cavity, a second tubal ring is loaded onto the applicator, and the same procedure is repeated for the opposite tube. The tubal ring not only occludes the lumen of the tube but also reduces the perfusion of blood through the doubled-over segment, resulting in ischemia of the strangulated loop.

Subjects

Only physically healthy women who requested sterilization for contraceptive purposes were selected as subjects. All women had terminated their last pregnancy at least six weeks before the sterilization. The age and parity distributions of the subjects are shown in Table 1. The mean age of the subjects was 32.3 years and the mean parity was 4.1 live births.

All patients were scheduled for a follow-up history and examination at 1 to 3 weeks, 6 months, and 12 months after sterilization. All but one subject returned for the 1- to 3-week and 6-month follow-up visits, and, as of May 1977, 83.2 percent of the subjects had returned for the 12-month visit.

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III. RESULTS

It was not necessary to complete any of the tubal ring procedures with an alternate method of tubal occlusion. Although some investigators (4) have reported the relatively frequent occurrence of tubal transection and mesosalpinx tears when tubal rings are applied, we have not found this to be a problem. Careful adherance to correct technique will obviate this problem. Before applying the tubal ring, the surgeon must be certain that each tube can be freely manipulated and is not adhered to other pelvic structures. After grasping the tube with the forceps, the laparoscope must be moved forward slowly as the tube is retracted into the inner cylinder of the laparoscope.

No serious complications necessitating hospitalization were experienced in any of the 291 tubal ring procedures; all patients were discharged from the hospital on the day of the procedure. Some patients experience mild to moderate pelvic pain for up to 48 hours after application of the tubal rings. However, the pain was adequately controlled with the administration of mild analgesics.

During the follow-up period, complications have been infrequently reported by the patients. For six patients (2.1%), complications related to the trocar incision have occurred, including separation of the incision, keloid formation, and infection. All of these complications were treated on an outpatient basis.

To date, 3 (1.0%) pregnancies have occurred among the 291 patients as a result of failure to occlude the Fallopian tubes. In two of these cases, the tubal ring had been applied to the broad ligament, and for the third case, it had been applied to the mesosalpinx. The pregnancies occurred at two, five, and six months after sterilization.

IV. COMMENT

From the results of this evaluation of 291 laparoscopic sterilization procedures with the application of tubal rings, it can be concluded that the procedure is safe and effective: there were no major complications, all patients were discharged from the hospital on the day of the procedure, and only three patients (1.0%) have become pregnant following sterilization. The three failures did not occur as a result of the tubal ring failing to achieve tubal occlusion, but as a result of application of the tubal rings to the broad ligament or mesosalpinx.

The safety and efficacy of using tubal rings at laparoscopy has also been demonstrated by other investigators (4, 5, 6). In using the tubal ring instead of electrocoagulation at laparoscopy, the patient is not subjected to the risks of abdominal burns. An added advantage of using tubal rings instead of spring-loaded and other types of clips is that when a tubal ring is inadvertently applied to the broad ligament or other improper structure, it can be removed by maneuverin it with the grasping forcep. A new ring can then be loaded onto the applicator and applied to the Fallopian tube. Spring-loaded clips cannot be removed after their application.

We have also evaluated the use of the tubal ring for tubal occlusion at laparoscopy after an induced abortion and after a normal term delivery, and have found the procedure to be satisfactory.

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TITLES AND LEGENDS

Table 1: **Title:** Age and Parity Distributions.

Legend: None.

Figure 1: **Title:** Tubal Ring Applicator and Close-Up Views of the Distal End of the Applicator.

Legend: Shown in the upper portion of the figure is the single-incision laparoscopic tubal ring applicator manufactured by KLI, Inc., 65 Industrial Drive, Ivyland, Pennsylvania, 18974. Shown in the lower portion of the figure is the grasping forceps in the extended position and the tubal ring fitted over the inner cylinder.

Figure 2: **Title:** Fallopian Tube After Application of the Tubal Ring.

Legend: None.

TABLE I

AGE AND PARITY DISTRIBUTIONS

AGE	NUMBER	PERCENT
20-29	97	33.3
30-39	171	58.8
40 and over	23	7.9
Mean	32.3	
PARITY		
1-2	43	14.8
3-4	156	53.6
5 and over	92	31.6
Mean	4.1	

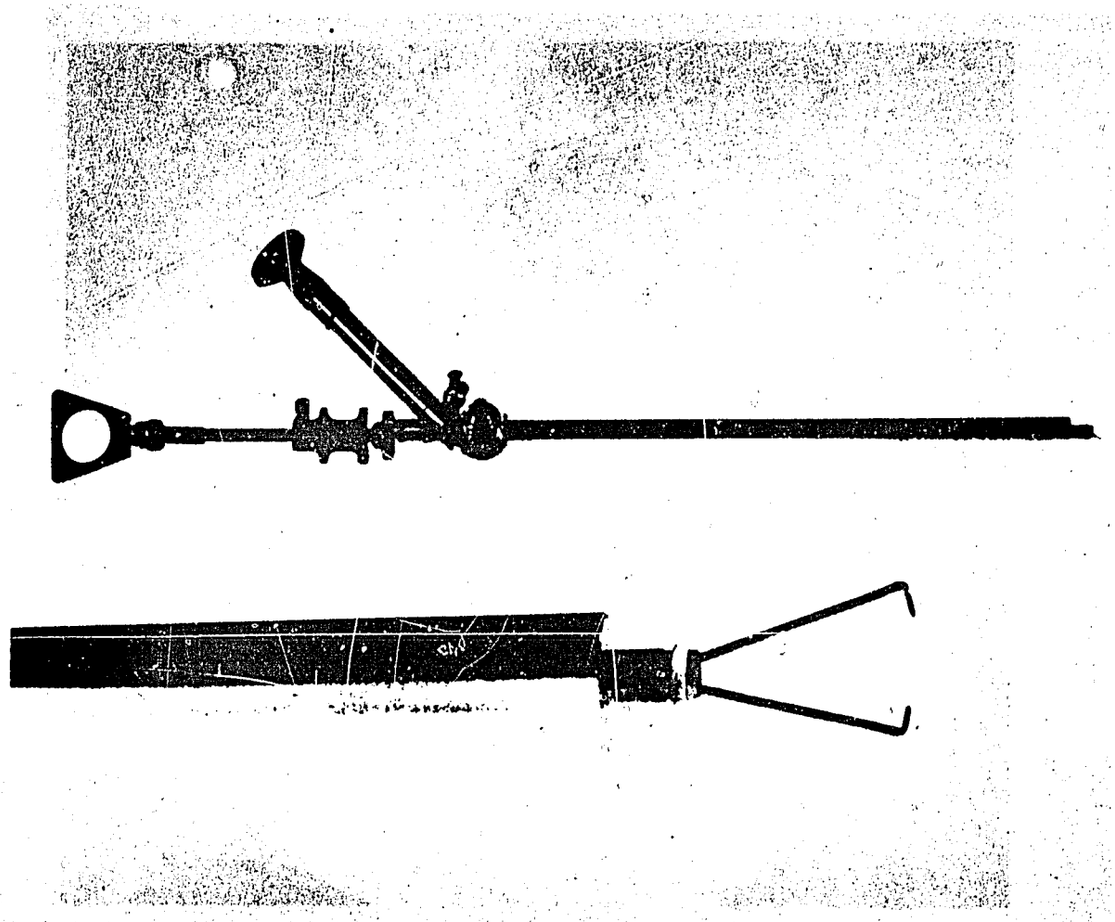

Figure 1. Tubal Ring Applicator and Close-Up Views of the Distal End of the Applicator.

Figure 2. Fallopian Tube After Application of the Tubal Ring.

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NONELECTRIC FEMALE STERILIZATION PROCEDURES AND THEIR POTENTIAL REVERSIBILITY

By

Leonard E. Laufe, MD

This work was supported in part by the International Fertility Research Program (AID/pha-C-1172).

INTRODUCTION

The potential for reversing female sterilization procedures depends on many factors. Voluntary sterilization patients should be selected carefully to minimize requests for reversals, which are major surgical procedures. Because a high rate of divorce and a variety of life styles exist in the United States and the United Kingdom, the stability of the patient's marriage or relationship should be evaluated as a mandatory requisite for elective voluntary sterilization in these countries. In countries and societies with high neonatal and early childhood death rates, the timing of the sterilization is critical. In many countries, for example, interval sterilizations to ensure the survival of the last born child are much more prevalent than postpartum procedures. Before assessing the various methods of tubal interruption or occlusion, one must appreciate the anatomy and physiology of the tube as well as what happens to the tube with each procedure. Every clinician must be aware that every technique of tubal interruption, transection, ligation, electrocoagulation, thermal burn, or the use of occlusive devices such as rings and clips was designed as a permanent method of sterilization and not as a reversible technique. The physician who provides tubal sterilization for his patients wants the operation to be failure-free and permanent. With these aims in mind, he can easily envision the tube merely as a conduit which allows the ovum to be fertilized and transported to its site of nidation. If he considers the concept of potential reversal, however, the physician must address himself not only to the technique of sterilization used, but to the site of injury and its effect on tubal physiology.

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PHYSIOLOGY OF THE TUBE

The Fallopian tube is not a passive uniform conduit. It is a dynamic functional organ with major variations in its anatomy - both gross and microscopic. It is capable of motility and has a rheology of its own. The tube is divided into three major portions with specialized functions. The infundibulum and delicate fimbria are mobile and capable of ovum pick-up. These structures and the soft patulous, thin-walled ampulla are lined with secretory and ciliated epithelium which move the ovum toward the ampullary isthmic junction of the tube (Figures 1 and 2). The ampullary isthmic junction is a critical area of the tube and is the site where fertilization occurs. Once fertilized, the gamete enters the muscular thick-walled isthmic portion of the tube where peristaltic activity completes the transport and delivery of the gamete to the endometrial cavity (Figures 3 and 4). Interference with the fluid dynamics of the tube, the ciliated epithelium, or ablation of the ampullary isthmic junction are major events which influence the potential for reversal with a resulting intrauterine pregnancy. The unique microanatomy and physiology of the human oviduct is best exemplified by the fact that the human is the only species in which ectopic pregnancies occur (Figure 5).

METHODS OF FEMALE STERILIZATION

Traditional methods

The traditional or classic methods of female sterilization are the Pomeroy with its many modifications, the Madlener, and fimbriectomy. These procedures can and usually are performed under local or regional anethesia,

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either postpartum or during an interval phase via minilaparotomy or colpotomy. In all instances, a portion of tube must be withdrawn through the incision and a segment of tube ligated and or excised. For the Pomeroy and Madlener techniques, the ampullary isthmic junction invariably seems to be ablated. Fimbriectomy seems simple, but removal of all of the fimbria is mandatory and the procedure is associated with a significant incidence of tubal-peritoneal fistulas and subsequent failures. Failures with the Pomeroy or Madlener are primarily due to recanalization.

These are the basic techniques which are being employed in the majority of the national programs throughout Asia. More complex procedures which require burial of a tubal stump in the leaves of the broad ligament require more skill, time, and anesthesia and have not achieved international popularity. The failure-free Uchida procedure with removal of the distal half of the tube is not a candidate for fertility restoration.

Laparoscopic Procedures

The majority of the laparoscopic procedures that have and are being performed utilize electrocoagulation. The lesion produced by the burn not only destroys the tubal wall, but can extend to the vascular arcades of the mesosalpinx. Unfortunately, the physician cannot know at the time of the burn how extensive the injury will be. When operating on patients with a previous laparoscopic sterilization, clinicians are frequently amazed to find how much of the tube and its supporting structures have been destroyed. Cases have been reported of ovarian atrophy when the burn injury extends to the ovary and its vasculature. The inability to

standardize the burn and subsequent tubal damage makes this technology one of the most difficult to correct if fertility return is requested.

One can readily appreciate that wherever the injury to the tube occurs, reversal implies that the defect must be corrected or bypassed. When the anastomosis is isthmic-isthmic or ampullary-ampullary, uniformity of diameter and wall thickness of the segments exists. However, when the anastomosis must be isthmic-ampullary or cornual-ampullary, the diameters and wall thickness of the segments have great disparity demanding more tedious repairs with poorer results. Implantation procedures are extended, bloody procedures and yield notoriously poor results.

Techniques and Devices for Tubal Occlusion

The first occlusive device which attracted attention was the tantalum clip. Gutierrez Najar of Mexico, using the culdoscopic approach, performed the operation on a large series of patients under local anesthesia on an outpatient basis. Unfortunately, the failure rate for these clips was high because they failed to maintain compression of the tube and showed subsequent propensity to migrate.

The major credits for developing effective technology that could be delivered through the laparoscope belong to I. B. Yoon of Johns Hopkins University for the silastic ring and J. Hulka of the University of North Carolina at Chapel Hill for the clip. The Hulka-Clemens clip, manufactured by the Wolf Company and modified by the Rocket Company, is a spring-loaded clip made of metal and plastic with jaws, which when closed provide a crushing injury to the tube (Figure 6). The clips are designed to maintain a constant pressure on the tubal wall. The silastic ring

(Figure 7) is an inert elastic device which, when stretched, allows a knuckle of tube to be drawn through it and then, when released, produces a constricting noose-like effect about the tubal segment. This produces an avascular necrosis and destruction of the tubal loop (Figure 8).

The primary intent of both these innovators was to produce a failure-free method of sterilization which would eliminate electrocoagulation procedures and their potential hazards. Neither Hulka nor Yoon set out to design a reversible method.

There are pros and cons for each technology. Although the area of injury is smaller with the clip, failures will occur unless it is placed at right angles across the isthmic portion of the tube. The ring technology destroys a larger segment of tube, approximately 1.5 cm, and this segment must contain a full thickness of the tube to avoid failure. When patients with these occlusive devices undergo a subsequent operation, the physician will find that either device will be covered with a filmy layer of peritoneum with minimal inflammatory response. Extrinsic tissue reaction to both devices is minimal and the area of injury is sharply demarcated for both devices.

Other occlusive devices must be evaluated. The Bleier clip is a self-locking plastic clip which has become popular in Germany (Figure 9). It has been used primarily via colpotomy with reported excellent results. Extensive international clinical trials through all routes must yet be performed to confirm the reported results and determine the incidence of long-term failures.

The ring concept has several variations. The Wolf Company has introduced a "blue ring" which is thicker than the Yoon fallope ring and has internal corrugations. The Eder Company recently exhibited a white ring which appears to be of a different consistency than the familiar Yoon device. Neither of these new rings has been adequately tested for elasticity, stress, or efficacy and, therefore, cannot be compared as yet with the fallope ring. Although their purpose is to accomplish safe and fool-proof permanent sterilizations, clinical experience with these devices is as yet too limited to be worthy of comment.

One little known surgical technique exists which is pertinent to the concept of potential reversibility. The Oxford technique (Figure 10) is a simple ligation transection of the tubal isthmus with fixation of the proximal and distal limbs on either side of the round ligament. These additional steps to the procedure require more anesthesia, a larger incision and more surgical expertise than the traditional minilap, rendering the Oxford technique currently unsuitable for many national programs. E. A. Williams of Oxford has reported successfully reversing 18 of 25 cases of previously sterilized patients with this technique by macrosurgical methods. This series appears to be a very selected group of patients and has yet to be replicated. If these results can be confirmed with other investigators under a variety of conditions, then the Oxford technique warrants critical international evaluation as a potentially reversible surgical procedure despite the drawbacks of the extra surgical maneuvers and expertise required.

COMMENTS

The interest in reversal procedures can be attributed to an increasing patient demand and the adaptation of microsurgical techniques to gynecologic procedures. The development and availability of operating microscopes and quality microsutures has opened surgical possibilities previously unexplored. The fundamental contributions of Winston of London in the development of improved instrumentation and surgical techniques have attracted worldwide attention and made successful microsurgical tubal repair a reality.

We have learned a valuable lesson from pelvic oncology. Radical pelvic surgery and intensive chemotherapy are best practiced in high-volume specific centers with trained personnel rather than in every community institution.

Gynecologic microsurgery must also be practiced in specialized centers with proper facilities, instrumentation, and trained personnel. Special surgical training and constant practice of the techniques are mandatory for the clinician involved. Interest in the procedures and performance of an occasional case do not lead to a successful program. Providing proper patient screening and follow-up must be a major activity. Accurate and detailed data collection and analysis are mandatory if continued progress is to be made. Successful tubal anastomosis can only be measured by the number of intrauterine pregnancies, not by patent tubes. The increased risk of ectopic pregnancies is a life-threatening complication for these procedures and the patients must be able to continually relate to a knowledgeable physician or institution.

Even with proper instruments, standards, and training, the critical question remains, "Which technique of tubal sterilization offers the greatest potential for reversal?". There is solid evidence that isthmic-isthmic and ampullary-ampullary anastomoses have higher success rates than procedures involving disparate segments. The isthmic portion of the tube is easier to work with due to its solid muscular wall. All of the occlusive technologies available, rings and clips and their variants, were designed for isthmic applications.

Although the rings destroy a larger segment of tube than the clips, their placement can be restricted to the isthmus. The choice of which device to use is a trade-off. The technical ease, patient acceptance, and efficacy of the original sterilization procedure must be weighed against the potential need for a reversal. At present, sufficient data is unavailable; however, certain conclusions can be reached. Occlusive devices are less traumatic than coagulation or excision procedures. Isthmic procedures offer better potential for reversal. Both rings and clips are candidates for resection. Careful selection of the low-parity patient for sterilization must be maintained to minimize the need for reversal procedures. More experience with reversal procedures is needed to answer many of the questions which can be raised. Perhaps the most obvious conclusion one can reach is the recognition of the tremendous need to pursue new technologies of sterilization which do not damage the tube and are truly reversible.

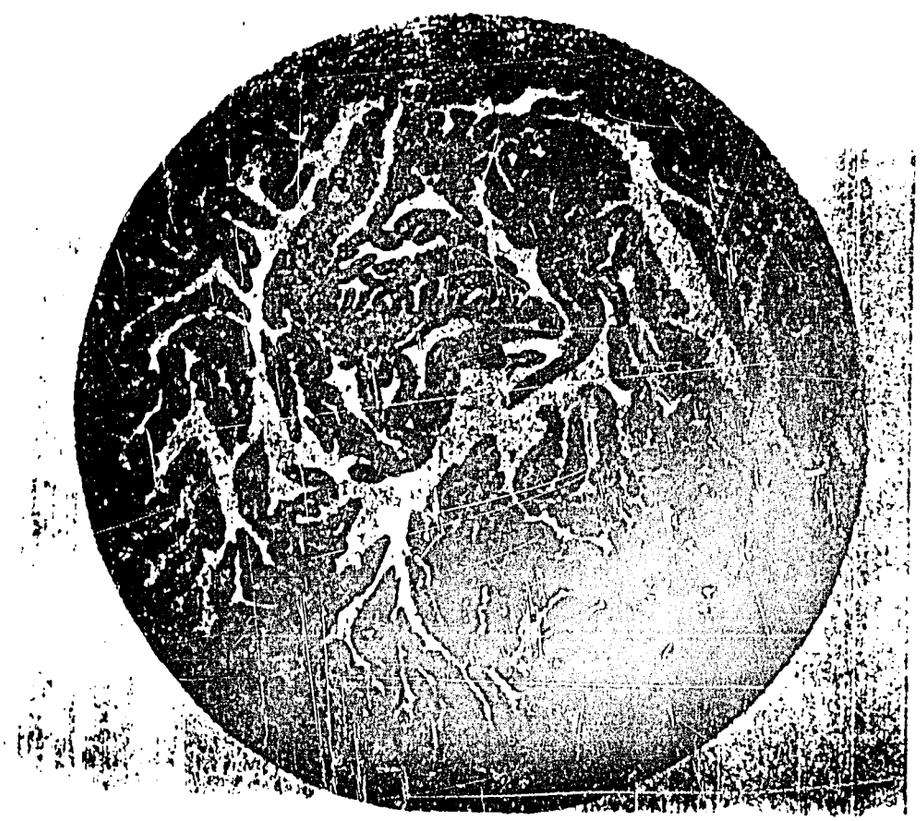


Figure 1. Cross Section of Ampullar.

From: Curtis, A H: A Textbook of Gynecology. W B Saunders Co., Philadelphia, 1946.

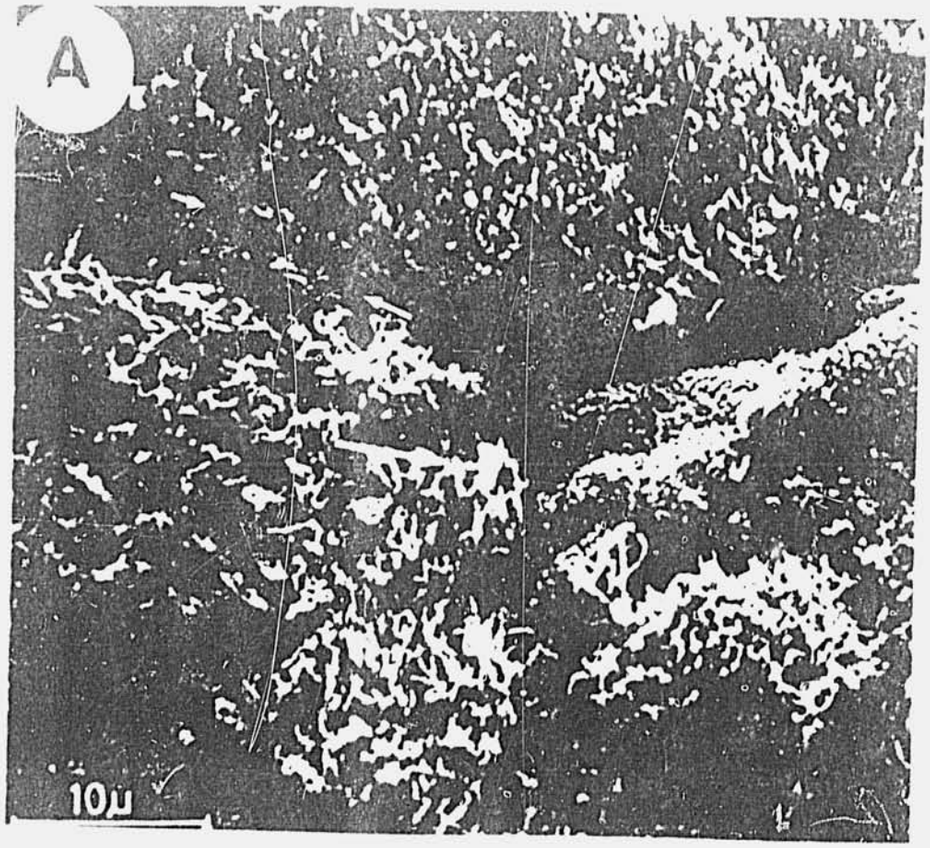


Figure [illegible]. Epithelial Pattern of Ampullar.

Source: [illegible], [illegible]. The Fallopian Tube: A Reappraisal. Lea and Febiger, Philadelphia, 1974.

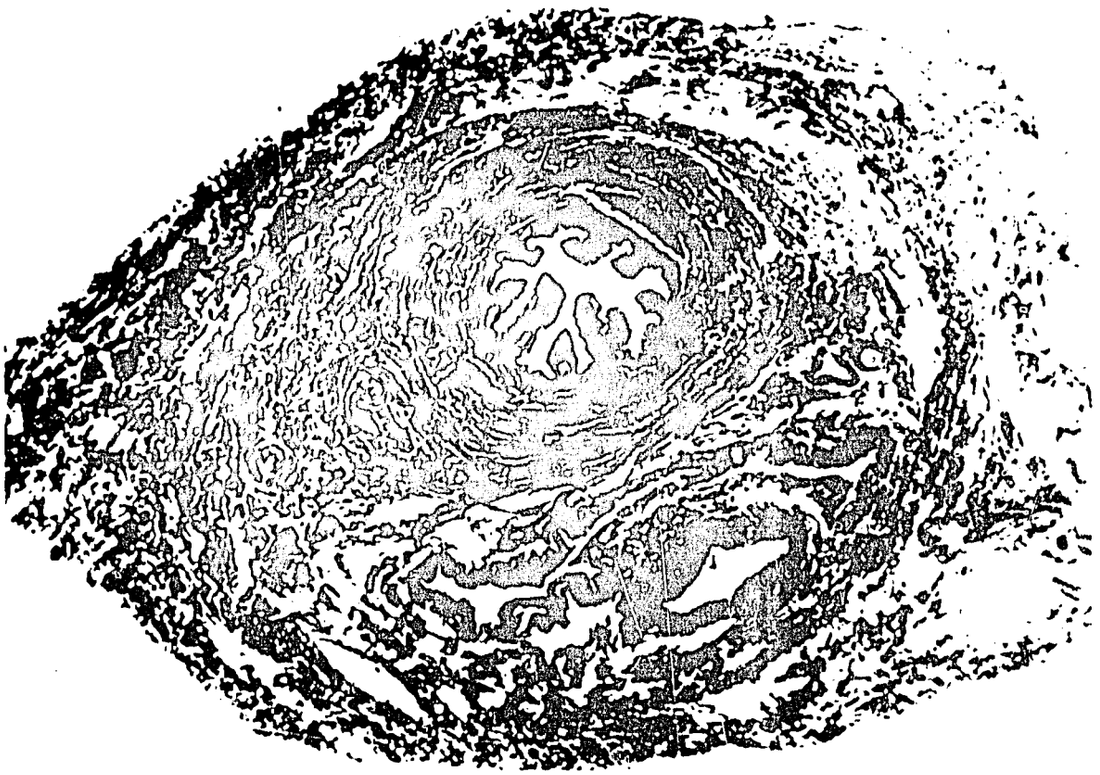


Figure 3. Cross Section of Isthmus.

From: Curtis, A H: A Textbook of Gynecology. W B Saunders Co., Philadelphia, 1946.

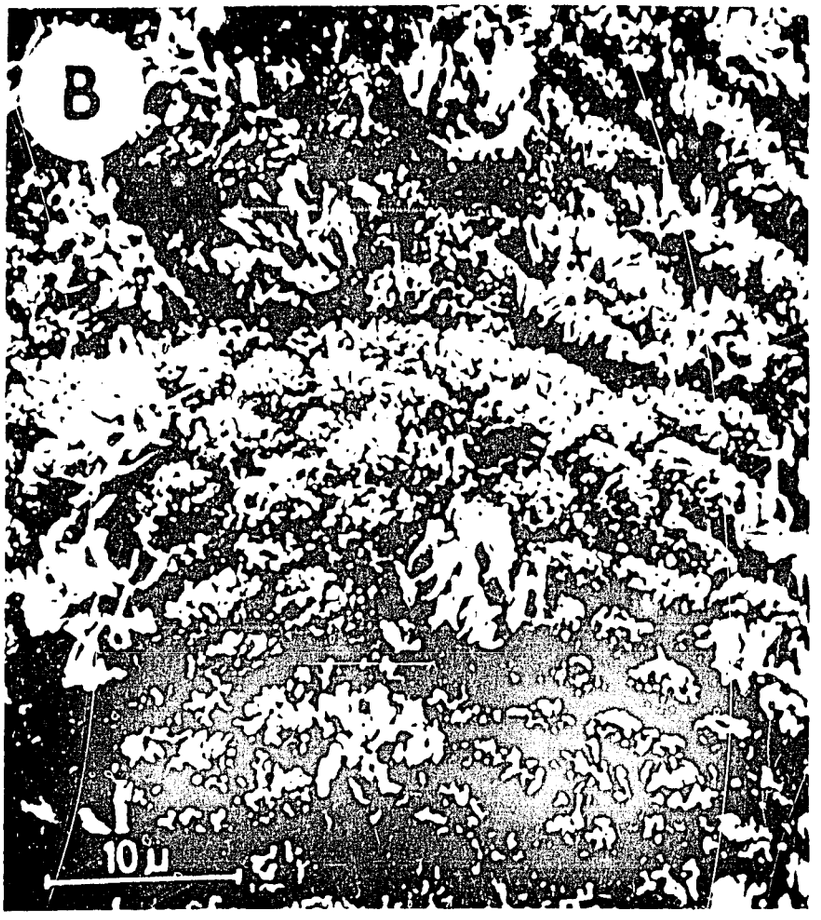


Figure 4. Epithelial Pattern of Isthmus.

From: Pauerstein, C J: The Fallopian Tube: A Reappraisal. Lea and Febiger, Philadelphia, 1974.

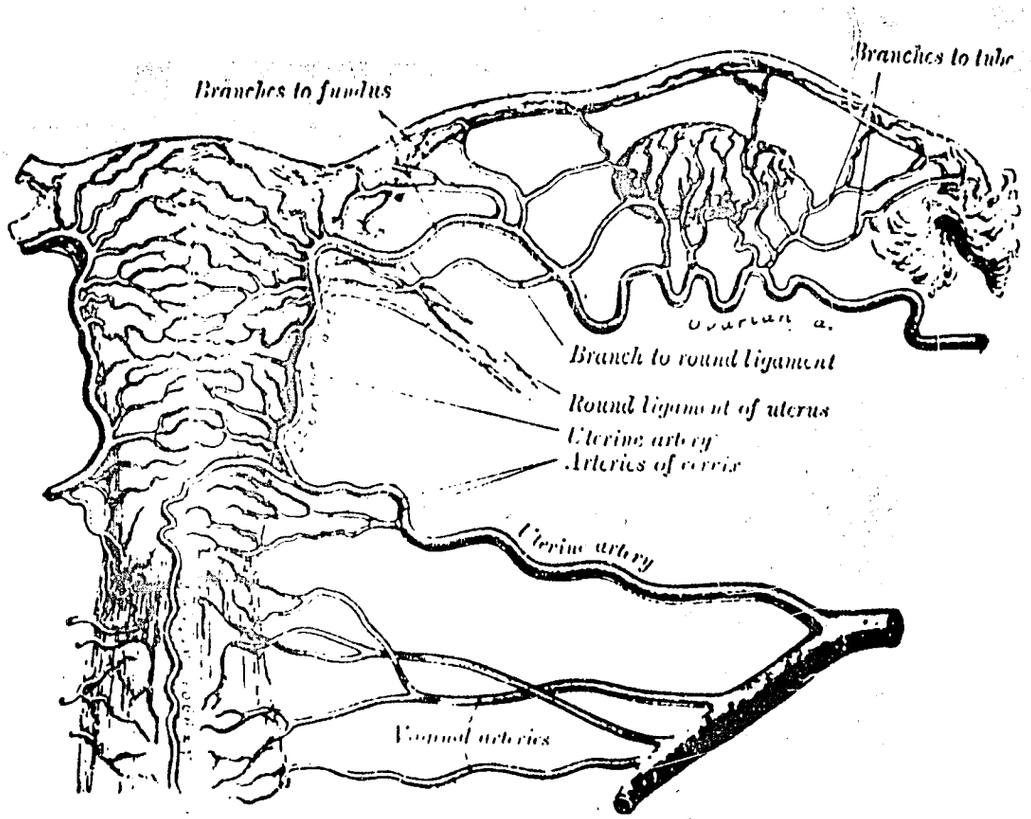
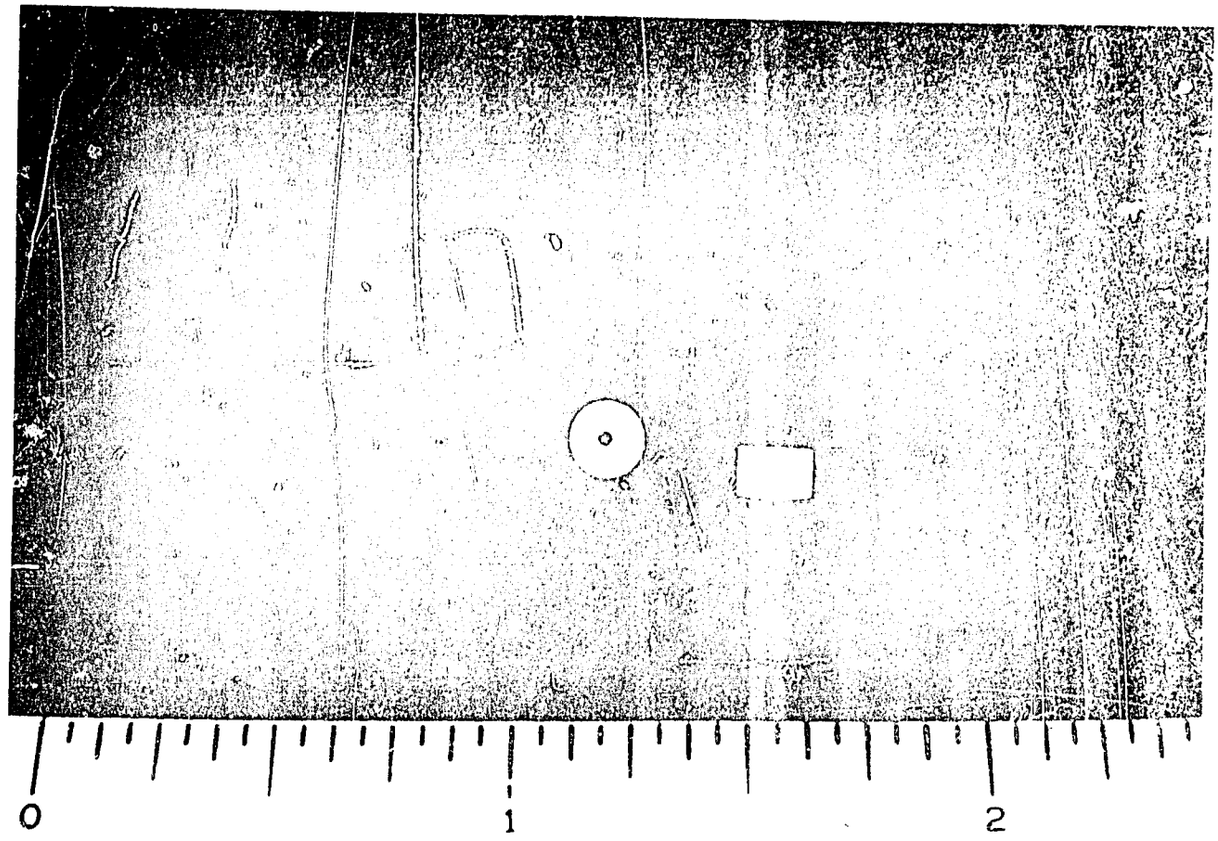


Figure 5. Vascular Supply of Tube.

From: Gray, H: Anatomy of the Human Body (ed. W.H Lewis). Lea and Febiger, Philadelphia, 1974.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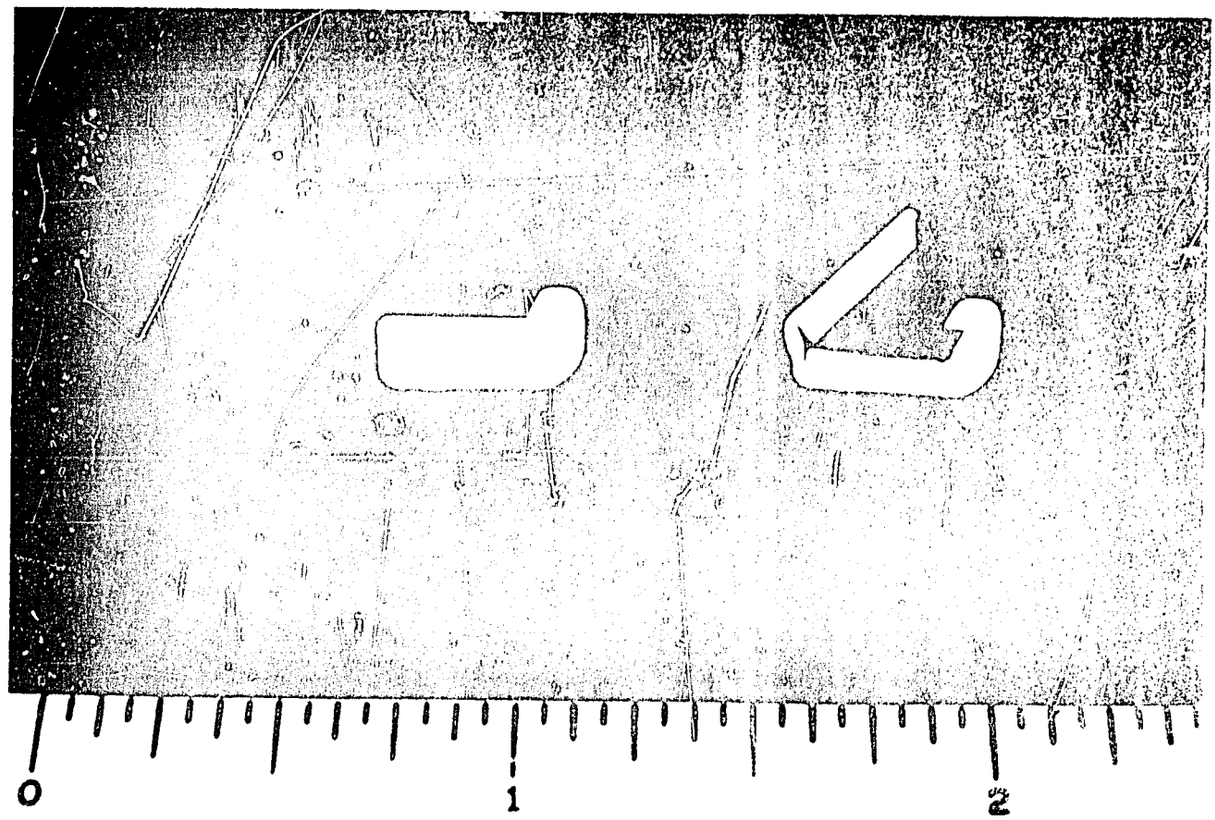
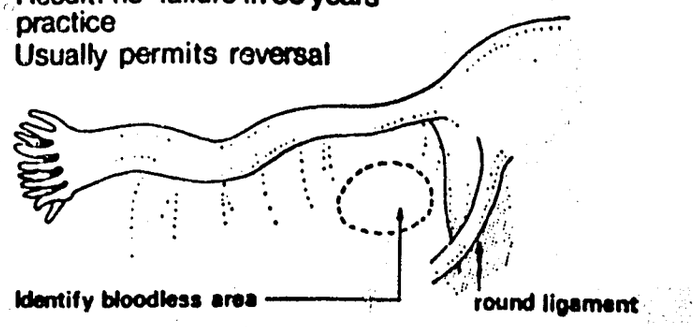
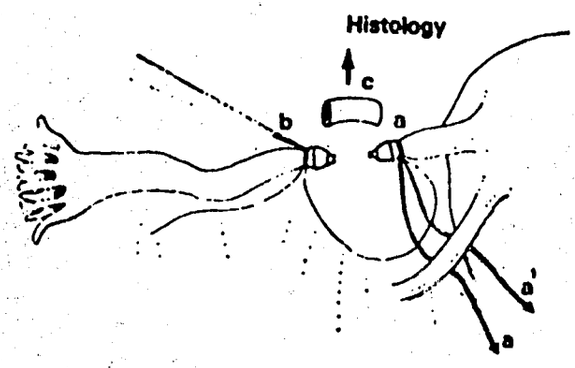


Figure 9. Bleter Clip.

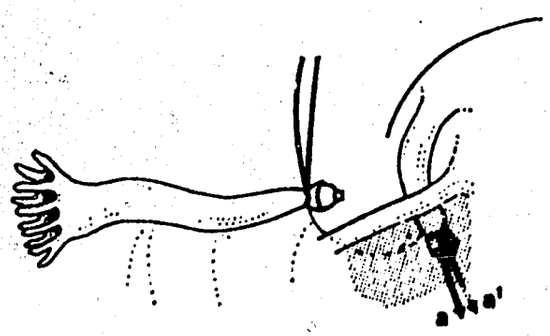
Oxford operation

Claim: physical separation of divided ends
Result: no failure in 35 years practice
Usually permits reversal

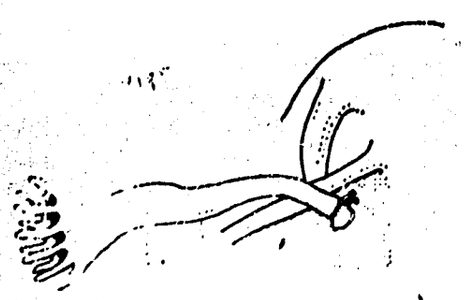




Tie a. no 1 catgut. Tie b. 35 thread. Pass a and a' separately under round ligament



Tie a and a' to secure medial portion oviduct behind round ligament



Tie a and a' to secure lateral portion oviduct in front round ligament. Operation completed.

Tissue: endometrium
excised portions of tubes

Figure 10. Oxford Technique.

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MINILAPAROTOMY--THE PROCEDURE

By

Leonard E. Laufe, MD

This work was supported in part by the International Fertility Research Program (AID/pha-C-1172).

INTRODUCTION

Interval outpatient minilaparotomy (minilap) has become the most frequently performed operation for voluntary female sterilization throughout the world. We are indebted to Dr. Vitoon Osathanondh of Thailand for developing special but simple instruments to facilitate the operation and help make popular the procedure. Minilap is most suitable for thin women and has become the operation of choice for national programs in Thailand, Bangladesh, and India.

Advantages of Minilap

Minilap offers numerous advantages over endoscopic or vaginal methods which more than compensate for the added discomfort to the individual patient. The operation can be performed under local anesthesia on an outpatient basis. It requires no sophisticated instrumentation and is performed under direct vision, and training for the procedure is minimal compared to that for endoscopic or vaginal techniques. An extensive surgical background is not necessary and the technique has been successfully taught to and practiced by paramedics. Immediate major surgical backup facilities are not required since the catastrophic complications possible with endoscopic techniques should not occur.

Basic Principle of the Operation

The basic principle of the operation is to elevate the uterine fundus against the parietal peritoneum at the suprapubic area making the tubes accessible through a small incision. A uterine elevator is used to accomplish this. The elevator designed by Vitoon is a uterine sound 28 cm in length with a cervical stop plate 5 cm from the tip to minimize uterine perforation (Figure 1).

The sound is angled proximal and distal to the stop plate for balance and thus, minimizes the possibility of the instrument falling out of the uterine cavity once inserted. The other instrument made popular by Vitoon is a right-angled tubal hook which is used to elevate the tubes through the incision when they are not easily accessible. A variety of other instruments will also serve to elevate the uterus, such as any insufflation cannula or Hulka's tenaculum sound. Tubal hooks have also been developed by Uchida and others and the author has modified the Vitoon hook so that the handle is angled and the loop for tubal elevation is curved to cradle the tube (Figure 2).

Despite the simplicity of the operation, some basic principles must be followed. Although minilap, like other interval procedures, can be performed at any time during the menstrual cycle, it is preferably carried out following a menstrual period to avoid a lateal phase pregnancy. If performed during the latter half of the cycle, one may simultaneously perform a menstrual regulation procedure. The bladder must be empty and a preoperative pelvic examination performed to ascertain uterine mobility and to rule out pelvic pathology. A fixed uterus should alert the physician to severe adhesive disease which can be a contraindication to the procedure.

Preoperative Medication

Preoperative analgesia-sedation is mandatory and should be administered slowly to avoid respiratory depression. The drugs most frequently used are a combination of Valium (10 mg) and pethidine hydrochloride (Demerol), 100 mg, given intravenously very slowly. Once the drugs are administered, the surgeon should wait at least five minutes to obtain the maximal therapeutic effect and

to allow the patient to stabilize. Although some physicians prefer to use other dosage schedules for intramuscular preoperative sedation 30 minutes prior to surgery, the intravenous combination described has worked exceedingly well in a variety of settings.

The cervix should be exposed with a speculum and cleansed with an antiseptic solution. A uterine elevating instrument is then inserted along the axis of the uterus. If the uterus is retroverted, it can be converted to an anterior position by a rotary motion of the elevator. Next, the lower abdomen is prepared for the surgical procedure, which includes shaving, scrubbing with a proper antiseptic, and using appropriate surgical drapes. The site of incision is selected approximately 2.5 cm above the upper margin of the symphysis or where the posterior margin of the fundus is palpated following uterine elevation. The site is then infiltrated with local anesthesia using either 0.5 or 1.0 percent xylocaine. A skin weal is raised and then the entire incisional site plus a surrounding margin of tissue is thoroughly infiltrated throughout all body layers. Usually 20 to 30 cc is sufficient to achieve proper anesthesia, but additional amounts can be used if the patient feels discomfort at any time. Waiting a minute or two will allow dissipation of the agent into the tissues to achieve proper anesthesia. The patient is then placed in the Trendlenburg position.

Operative Procedure

A transverse skin incision is made at the selected and anesthetized site. The incision should be 2.5 cm in length for thin women and slightly larger for patients who are more obese. The subcutaneous tissue and rectus sheath are also opened transversely with the operator using care not cut the underlying rectus muscles. The underlying pyramidalis and rectus muscles are dissected free

of the sheath for at least 1.5 cm above and below the incision. The midline is identified and, with blunt dissection, vertically spread open for 2.5 cm.

The uterus is elevated until the peritoneum is bulging and the operator is certain that the urinary bladder is not in the surgical field. The peritoneum is grasped with hemostats, elevated, and opened vertically for at least 2 cm. Small right-angle retractors can then be inserted or a specifically designed self-retaining retractor may be employed (Figure 3). Although the Madrigal modified vaginal speculum and an anscope are employed by some proponents of minilap, most experienced operators find these two instruments cumbersome and confining. If the self-retaining retractor or small right retractors are used, a surgical field of about 2.5 cm square is created which is more than adequate for the operation.

The pelvic contents are visualized and any omentum over or in front of the uterus is moved toward the upper abdominal cavity with a blunt instrument. The uterus is again elevated toward the peritoneal opening and moved laterally so that both the right and left tubes are visualized and become accessible.

Each tube in turn is grasped with a nontraumatic forceps, such as a Babcock, and brought out through the incision. Frequently the experienced minilaparotomist can bring the tube out by a digital technique. The index finger is placed on the posterior leaf of the mesosalpinx and then gently raised to hook the tube upward. If the operator experiences difficulty in either digitally or directly picking up the tube, the tubal hook can facilitate this step of the operation.

The Pomeroy procedure is the one most frequently employed for sterilization. Recently there has been great interest in the use of occlusive devices, such as rings and clips. Occlusive devices can save time, produce a standard trauma to

the tube, and, most important, can be applied within the pelvis to minimize patient discomfort. To accomplish the intrapelvic application of an occlusive device, retraction is mandatory, and the self-retaining retractor was designed for this purpose.

Once both tubes have been ligated or occluded and hemostasis ascertained, the wound is closed. This must be accomplished in anatomic layers. Standard absorbable sutures are used for the peritoneum, fascia, and subcutaneous layers. Some surgeons prefer a purse string suture for the peritoneum and interrupted sutures for the fascia, while others will use a continuous technique. For thin patients, two or three skin sutures which include the subcutaneous fat are all that is necessary. For more obese patients, these layers should be closed individually. The majority of minilaparotomists, particularly in the developing countries, use silk sutures for the skin so that the patient must return for the follow-up visit to have the sutures removed. The wound is then covered with an appropriate dressing.

Postoperative Care

The patient should be observed for a minimum of two hours following the surgery. Ordinary oral analgesics usually control the discomfort of the first 24 hours. In most of the large-scale camp programs being conducted throughout Asia, the patients are observed until they void and expel flatus. Although liquids and soft foods are offered at a patient's request, solid food is not given until normal intestinal motility has been determined. Prophylactic antibiotics are not employed. The most frequent complications observed are wound infections which are confined to the subcutaneous layer and respond to antibiotics or drainage.

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Minilaparotomy is usually accomplished in 15 to 20 minutes which allows adequate time to perform the procedure in a precise, orderly, and gentle manner. The observer is amazed at how quickly most patients ambulate and return to a normal routine. The simplicity of minilaparotomy, its acceptability, its feasibility under a variety of settings, its independence of complex instruments and sophisticated technology and training, and the accompanying low complication rate have made this approach to female sterilization the operation of choice in many countries throughout the world.

TITLES AND LEGENDS

Figure 1:	**Title:**	Vitoon uterine elevator, above, and Vitoon uterine hook.
Figure 2:	**Title:**	Modified hook by Laufe and Vitoon hook.
Figure 3:	**Title:**	Laufe Self-Retaining Retractor.

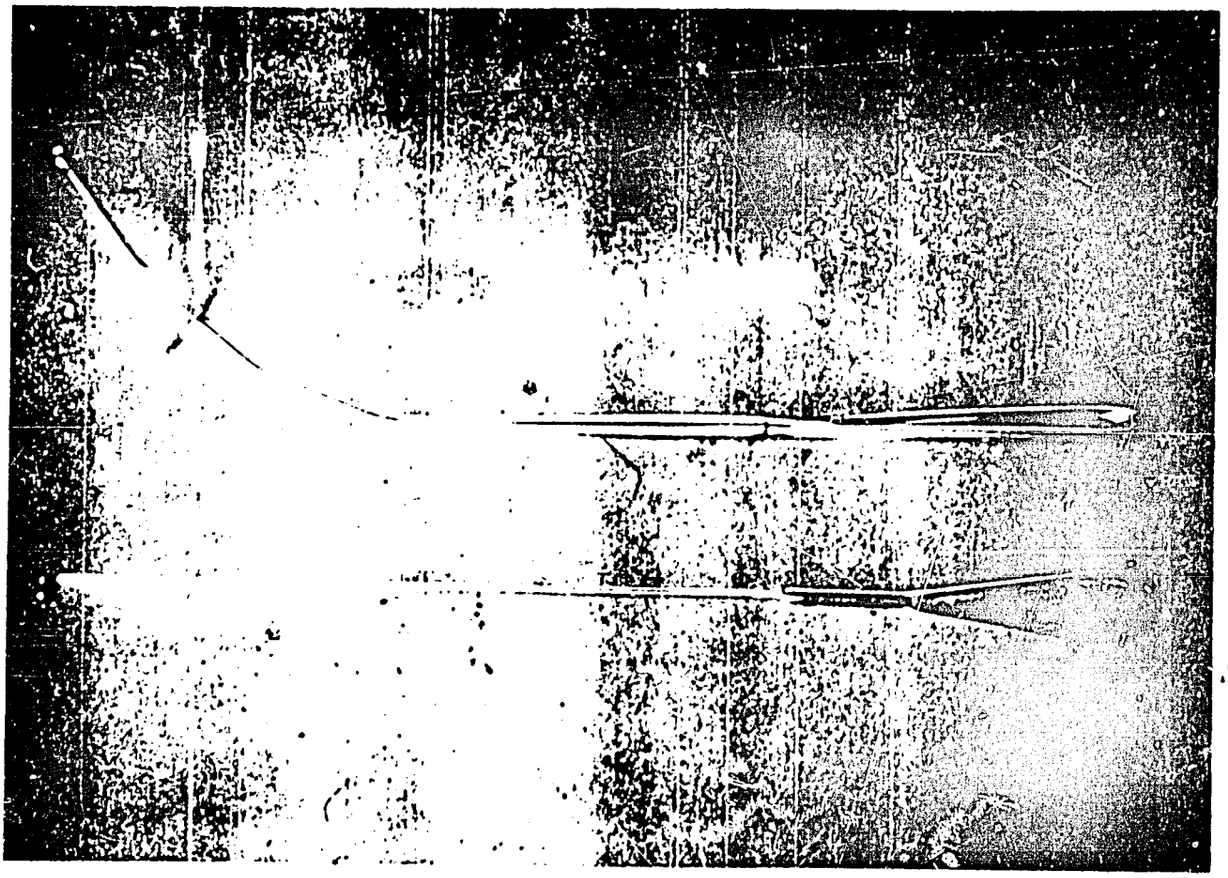

Figure 1. Vitoon uterine elevator, above, and Vitoon uterine hook.

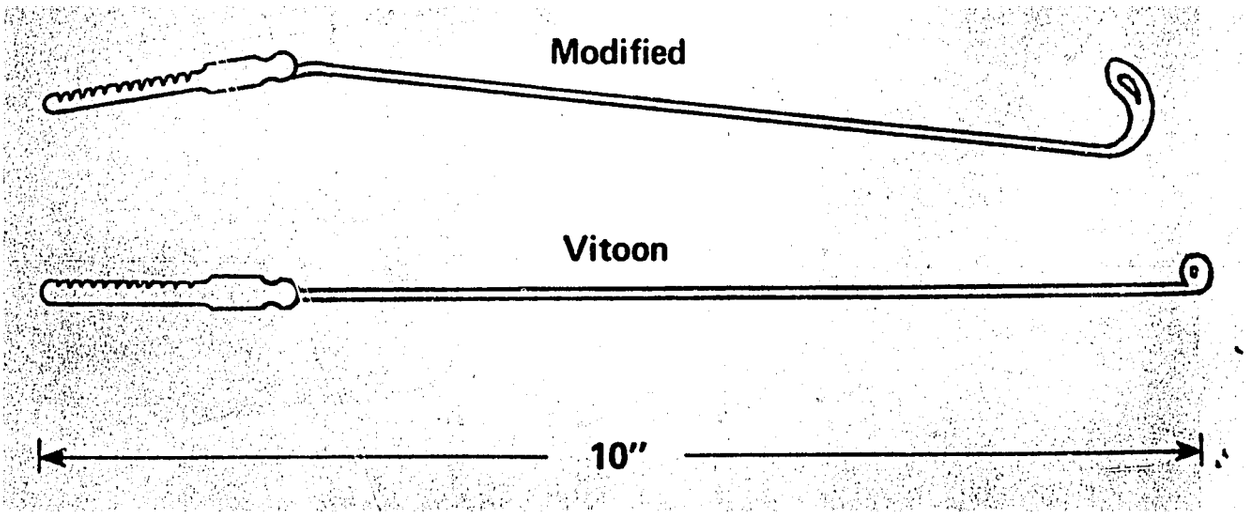

Figure 2. Modified hook by Laufe and Vitoon hook.

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(Ginec. Obtet. Méx.)
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Núm. 248 Junio, 1977

EL ANILLO DE YOON EN EL POSTPARTO INMEDIATO[1]

Reporte preliminar

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DR. RODOLFO MUÑOZ R.**
México, D. F.

LA APLICACIÓN de los anillos de silastic para lograr la oclusión tubaria en pacientes con antecedente obstétrico lejano, es una técnica que se realiza cada vez con más frecuencia,[2, 4, 6] particularmente con control laparoscópico, puesto que ha eliminado las serias complicaciones de la electrocoagulación tubaria. Los resultados comparativos han sido satisfactorios en lo que a efectividad se refiere, pues en un grupo de 5,508 pacientes[2] en las que se emplearon las técnicas de coagulación, clip y anillo de silastic, los porcentajes fueron 0.04, 1.2, 0.02 respectivamente. Las complicaciones más serias fueron quemaduras de asas intestinales y sólo se observaron en el grupo de electrocoagulación. Las dificultades técnicas más frecuentes fueron con el clip de Hulka y la mayor sencillez de aplicación con el anillo, además en este grupo las complicaciones fueron de mínima significación.

Con frecuencia se ha repetido en las reuniones médicas que los anillos de silastic no son aconsejables en el postparto inmediato, por las modificaciones de volumen y vascularización de los órganos genitales internos durante la gestación; se ha insistido en que el grosor de la trompa de Falopio es tal, que no permitiría la aplicación de el anillo, que el aplicador provocaría frecuentemente la sección tubaria y esto podría ser causa de sangrado de mas o menos consideración. La experiencia mundial que se tiene en la técnica quirúrgica mencionada es muy limitada.[1] Por estas razones nos propusimos evaluar la aplicación de el anillo de silastic en el postparto inmediato.

La experiencia[3] de el trabajo realizado en el Hospital de Gineco-Obstetricia No. 2 en pacientes en las que el antecedente de gestación no era

Hospital de Gineco-Obstetricia del Centro Médico Nacional, I.M.S.S.
* Director.
** Médico Gineco-Obstetra de Base.
[1] Este trabajo fue realizado por la participación del International Fertility Research Program.

reciente y el conocimiento adquirido en una enferma de las modificaciones tubarias posteriores a la intervención, a la cual se le aplicó el anillo de silastic en julio de 1975 y que fue motivo de una histerectomía total abdominal en diciembre de 1976 por anomalías de sangrado uterino, nos demostraron que la técnica de salpingoclasia por el anillo de Yoon, ya sea con control laparoscópico a través de una minilaparotomía es sencilla y confiable y pudimos observar en el espécimen quirúrgico de la paciente mencionada, que la luz tubaria estaba modificada completamente en el asa que se encontraba por encima de el anillo aplicado, con fibrosis, hialinización, calcificación o en pequeñas zonas con inflamación crónica focal; la oclusión tubaria se hace por intermedio de tejido conjuntivo fibroso, con hialinización y desaparición de la mucosa tubaria (Figs. 1 y 2).

Con estos conocimientos previos planteamos la conveniencia de aplicar los anillos en pacientes cuyo parto hubiera sucedido en un lapso no mayor de 24 horas atendidas en el Hospital de Gineco-Obstetricia de el Centro Médico Nacional.

MATERIAL Y MÉTODO

Se seleccionaron 110 pacientes en el puerperio inmediato cuya caracte-

FIG. 1. Sección de trompa derecha en la porción comprimida por el anillo. La luz tubaria ocluida por tejido conjuntivo fibroso. Paciente operada 16 meses después de la salpingoclasia por la presencia de un pólipo endocervical.

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FIG. 2. Otra sección mostrando una banda de calcificación periférica

rística genérica fue el haber tenido su parto como máximo, 24 horas antes de la operación proyectada y haber solicitado en forma voluntaria el control permanente de su fertilidad futura, la solicitud fue hecha por escrito con la firma de los dos cónyuges. La edad promedio de las pacientes operadas fue de 31.1 años las características de sus partos fueron:

Eutócicos	95
Pélvicos	2
Fórceps	2
Conducción	2
Ext. Manual de placenta	1
Revisión de cavidad	8

El número promedio de gestaciones fue de 5.5 distribuido como sigue:

Gestaciones	Núm. de pacientes
2 a 5	62
6 a 10	32
11 a 14	16
TOTAL	110

El numero total de abortos en estas pacientes fue de 66 lo que significa un promedio de 0.6, el máximo de abortos en una paciente fue de 5. El total de niños vivos en el grupo es de 613, con promedio de 5.1, la paciente con mayor número de hijos fue de 13 y la cifra más baja fue de 2 en una enferma cardiópata que ameritó una valvuloplastía.

La anestesia en la gran mayoría fue el bloqueo epidural, aprovechando en el 52% de ellas, la continuidad del método empleado durante el trabajo de parto; en 12 de ellas, la anestesia general fue la indicada y en tres, fue necesario agregar al bloqueo la anestesia general, por falla del primer procedimiento.

La técnica quirúrgica fue la siguiente:

Incisión horizontal de dos a cuatro centrímetros de longitud dependiendo del espesor del panículo adiposo, a nivel de el fondo uterino, localizado por palpación.

Incisión horizontal de la hoja anterior de la aponeurosis de los rectos y de la línea alba, sección del peritoneo y separación de la apertura con separadores de Farabeuf o similares.

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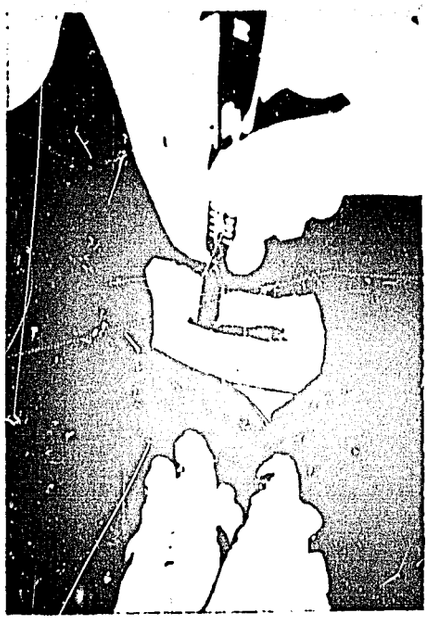

Fig. 3. Incisión transversal de piel, tejido celular, aponeurosis y peritoneo.

Localización de la trompa de Falopio, ayudándose con el desplazamiento contralateral del útero y la movilización de la salpinge con el dedo o con una torunda de gasa.

Toma de la trompa con una pinza de Babcock o con los ganchos del aplicador del anillo. Si el primer procedimiento es el empleado, se fija la trompa con los ganchos del aplicador, a dos y medio centímetros de la porción cornual, cuidando de no incluir en ello los vasos del mesosalpinx, se desliza el anillo de silastic para dejarlo colocado en la trompa y se repite el procedimiento en el lado opuesto (Figs. 3 y 4).

En este grupo se emplearon tanto el aplicador sencillo como el doble (Figs. 5 y 6).

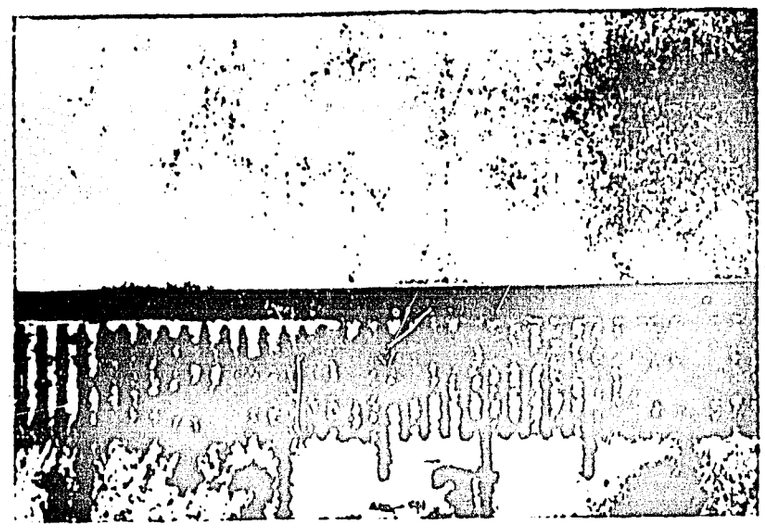

Fig. 4 Anillo de Silastic

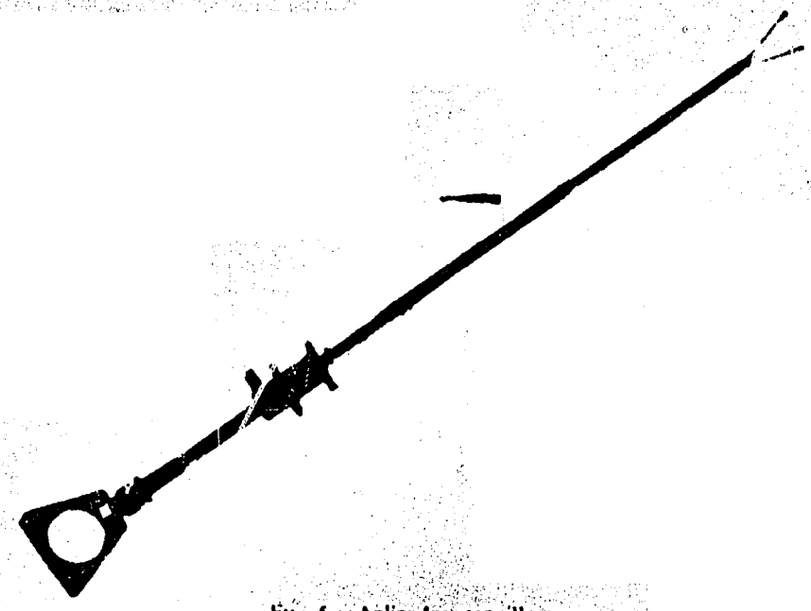

FIG. 5. Aplicador sencillo

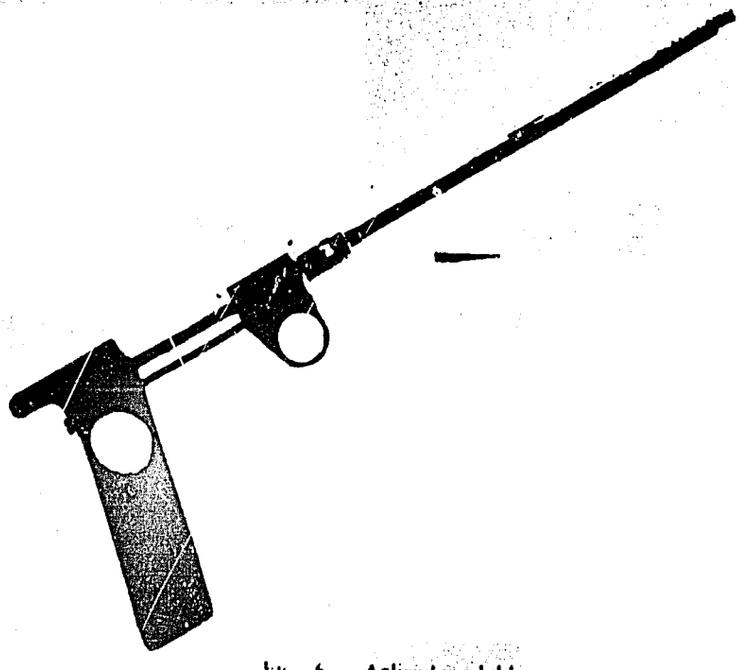

FIG. 6. Aplicador doble.

El tiempo transcurrido entre el parto y la intervención quirúrgica fue de 30 minutos a 24 horas como máximo.

El procedimiento se realizó, únicamente en aquellas pacientes en las que hicieron solicitud escrita, firmada por ambos cónyugues y en el 82.1%, esta petición se basó en la multiparidad, que varió entre tres y trece hijos vivos, aunque con el mismo concepto de grupo familiar al considerar que el número de hijos era suficiente para cada uno. En las otras pacientes hubo indicación médica además de la solicitud requerida, patología cardíaca, diabetes y problemas de isoinmunización, fueron las principales causas.

Resultados

El procedimiento planteado fue realizado en todas las pacientes programadas para ello, independientemente de sus características somáticas o patología agregada.

Encontramos en la cavidad abdominal, en todas ellas, líquido seroso de trasudado peritoneal en cantidad variable, que en algunas pacientes toxémicas fue excesivo y dificultó un poco la localización de las trompas de Falopio, maniobra que en general es fácil, pero debe realizarse con suavidad para evitar traumatismos innecesarios.

Inicialmente, fijamos la salpinge con pinzas de Allis antes de colocar el aplicador, en dos pacientes se desgarró moderadamente la serosa peritoneal y por ello empleamos posteriormente las pinzas de Babcock, que evitan el desgarro, preferimos hacer tracción moderada con la pinza de Babcock para evidenciar más fácilmente el espacio que separa los vasos dilatados del mesosalpinx durante la gestación y la pared tubaria, con el objeto de evitar el hematoma por desgarro vascular al lesionarlos con los ganchos del aplicador, complicación que debe evitarse siempre por la rapidez con la que el hematoma que se forma, separa las hojas de el mesosalpinx y requiere una hemostasia inmediata. Se empleó el aplicador sencillo en 78 pacientes y en las 32 restantes el doble. La aplicación del anillo de silastic se facilita con el aplicador sencillo en parte porque el diámetro de la luz del tubo metálico es un poco más amplia y por la sencillez de su manejo. El aplicador doble tiene algunos inconvenientes la longitud excesiva del mango de madera y la cercanía del orificio que tiene para apoyar el pulgar al deslizar el tubo metálico externo para aplicar el anillo, lo que obliga a cambiar de posición la mano, ello provocó en dos casos la expulsión prematura del anillo, que quedó fijando los ganchos metálicos, pues aun no se había introducido la trompa.

En dos pacientes hubo sección tubaria con los ganchos del aplicador al momento de introducirla en la luz del tubo metálico, en ellas, se empleó el aplicador doble.

Las complicaciones transoperatorias fueron dos hematomas de la pared

tubaria, provocados al desgarrar la serosa con la pinza de Allis, ambos fueron de poca magnitud y se controlaron al aplicar el anillo. La única complicación tardía fue una celulitis en el sitio de la incisión.

La estancia hospitalaria no se modificó, puesto que el 98% requirieron de 24 a 48 horas y 3 de las pacientes permanecieron 3, 7 y 12 días, por celulitis de la pared abdominal la primera y complicación del procedimiento anestésico las dos restantes (cefálea persistente).

Las pacientes fueron vistas antes del décimo día postoperatorio y en ninguna de ellas se observó modificación alguna. El control a largo plazo, nos informará con propiedad de la efectividad ya que ha transcurrido poco tiempo desde la fecha en que se hizo la última operación de este grupo.

Comentario

Apoyadas en la experiencia anterior[3] de nuestras pacientes operadas con antecedente lejano de embarazo y parto, así como la expuesta por otros autores,[2, 6] consideramos que aunque el grupo estudiado es poco numeroso, permite señalar que la técnica de aplicación del anillo de silastic en las pacientes en el postparto inmediato, es sencilla y sin complicaciones significativas, si se siguen con cuidado las indicaciones generales de cirugía: manejo suave y cuidadoso de los elementos anatómicos, evitar tracciones exageradas, colocación del anillo en la unión del tercio proximal con el medio de la trompa.

Incrementaremos en el futuro el número de las pacientes operadas y esperaremos el tiempo suficiente para informar de la técnica en función de meses de exposición, convencidos de la bondad del procedimiento.

Summary

Our experience shows that the silastic ring application during the immediate post-partum period is simple and without important complications, if general indications are followed, gentle handling, to avoid traction, and ring application in the proximal third of the tube. In the future, with more patients treated we will be able to evaluate the results on bases of months of exposure.

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MALE STERILIZATION SERIES
NO. 2

INTERNATIONAL FERTILITY RESEARCH PROGRAM
CONFERENCE PAPER

MALE STERILIZATION IN GUATEMALA

By

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Guillermo Escobedo, MD
John S. H. Elkington, PhD
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MALE STERILIZATION IN GUATEMALA

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Abstract

MALE STERILIZATION IN GUATEMALA

By

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It is sometimes stated that vasectomy is not acceptable to men in Latin America because of various cultural factors. This report uses socio-demographic and clinical data related to vasectomy of 986 men who were sterilized from 1973 to 1975 at the Asociación Pro-Bienestar de la Familia de Guatemala to assess the acceptability of male sterilization in this Latin American population. The mean age of these men was 34.8 years and they had an average family size of 4.2 children. The average educational attainment of the patients was 6.5 years. Most men represented one of four major occupational groups including skilled workers (42.7%), unskilled workers (33.2%), professionals (9.3%), and craftsmen (6.5%). The number of men requesting vasectomy during this study increased from 14 per quarter in 1973 to more than 100 per quarter after mid-1974. This fact, together with the lack of complaints after the operation, the rate of patient referrals by vasectomized men (8.3%), and the time taken to resume intercourse (most resumed intercourse within a week after the operation) indicates that vasectomy is acceptable to men in Guatemala.

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I. INTRODUCTION

In comparison with methods of female sterilization, male sterilization by vasectomy is a relatively inexpensive and minor surgical procedure[1,2]. It may be the method of contraception chosen by men where the desired family size has been attained and other contraceptive methods are inconvenient, have undesirable side effects, are expensive or are unavailable. Since vasectomy is essentially an irreversible procedure, much work has been done to investigate the reversibility of the procedure and any physiological and psychological changes resulting from the operation[2-6].

This paper reports some data from a series of Guatemalan men who were sterilized by vasectomy at the Asociación Pro-Bienestar de la Familia de Guatemala in order to define the socio-demographic profile of the group and to obtain an estimate of the acceptability of the operation. The included clinical data indicate that vasectomy is essentially free from complications.

II. MATERIALS AND METHODS

Procedure

Vasectomy was performed by first preparing the scrotum with soap and water and antiseptic solution and then infiltrating it with a local anesthetic (1% lydocaine) above the spermatic cord. The vas deferens was located through a scrotal incision. A portion of the vas deferens was excised (10-12 mm), and the cut ends ligated with chromic catgut (80.2% of patients), silk (16.4% of patients), or nylon (0.9% of patients). In most of the patients this operation took from 11 to 20 minutes (95.0%).

Data Collection

Socio-demographic and clinical data were collected on standard forms developed by the International Fertility Research Program. A series of questions from these forms has been used to determine the motivation for sterilization, its acceptability, and any disruption the operation may have caused in the sex life of the patient. These questions are:

1. Primary referral source

   Self or wife
   Family planning staff
   Private physician
   Other agency
   A previously vasectomized man
   A man not previously vasectomized

2. Primary reason for choosing sterilization

   Other methods:
     Unavailable
     Unreliable
     Undesirable side effects
     Inconvenient
   Other reasons

3. Complications, complaints and pain at surgery and follow-up

4. Time until the resumption of intercourse

III. RESULTS

Most of the men lived in an urban area (93.1%), were Roman Catholics (83.0%), and were currently or formerly married (98.7%). Table I shows that most of the men were from 25 to 44 years of age. Half (49.7%) were 25 to 34 years old and 37.5 percent were 35 to 44. Their mean age was 34.8 years.

The mean educational level for this population was 6.5 years: 24.9 percent had less than 4 years of education, about 40 percent had 4 to 6 years of education, and 35.1 percent had more than 6 years of education. More than half of the men (65.7%) had 4 or fewer children (Table II); 10.7 percent had more than seven children. The mean family size was 4.2 children.

Most of the men in this study fit into four major occupational groups: skilled workers (42.6%), unskilled workers (33.3%), professionals (9.3%), and craftsmen (6.3%) (Table III). Only 0.4 percent of the population were unemployed at the time of the procedure.

TABLE I
AGE AND EDUCATIONAL STATUS OF 986 MEN UNDERGOING VASECTOMY

	No.	%
Age (years)		
Less than 25	35	3.6
25-34	490	49.7
35-44	369	37.5
45 or more	92	9.3
Mean	34.8	
Education (years)		
None	59	6.0
1-3	186	18.9
4-6	393	39.9
7-9	156	15.8
10 or more	190	19.3
Unknown	2	0.2
Mean	6.5	

TABLE II
FAMILY SIZE FOR 986 MEN UNDERGOING VASECTOMY

Number of Living Children	No.	%
1-2	134	13.6
3-4	514	52.1
5-6	232	23.5
7+	106	10.7
Mean	4.2	

TABLE III
OCCUPATION OF 968 MEN UNDERGOING VASECTOMY BY CONTRACEPTIVE PRACTICE OF THE COUPLE

	Occupation					
Contraceptive	**Skilled Worker** *(N = 421)*	**Unskilled Worker** *(N = 328)*	**Professional** *(N = 92)*	**Craftsman** *(N = 64)*	**Other** *(N = 81)*	**Total*** *(N = 986)*
Orals	65.3	63.7	64.1	53.1	59.3	63.4
None	14.7	19.5	7.6	18.8	19.8	16.3
Condom or spermicide	7.4	7.0	9.8	10.9	4.9	10.2
IUD	6.9	4.9	8.7	7.8	6.2	6.4
Injectable	1.2	1.2	5.4	0.0	1.2	1.7
Other	4.5	3.7	4.3	9.3	8.6	2.0
Total*	**42.7**	**33.3**	**9.3**	**6.5**	**8.2**	

** Percent of the total number of patients.*

The relationship between occupation and contraceptive methods used before sterilization is shown in Table III. Non-use of contraceptives was reported by 7.6 percent of the professionals compared with 14.8 to 19.4 percent of the other groups of men. More than half (53.1 to 65.3 percent) of the men in each occupational group reported that their wives had used oral contraceptives.

Table IV shows that there were two main sources of information about the availability of vasectomy for the men in this study. Family planning staff (49.4%) and men who had not had a vasectomy (25.9%) accounted for the majority of the referrals in this study; private physicians and vasectomized men accounted for 15.2 percent of the referrals. Almost half of these men (47.9%) chose sterilization in preference to other methods of contraception because temporary methods had undesirable side effects (Table V). A further 47.9 percent of the men stated that they had completed their family size, a reason for wanting contraception but not a reason for preferring vasectomy over other methods of contraception. (This indicates that the men wanted a long term, permanent method of contraception and that vasectomy fulfills that condition.)

TABLE IV
REFERRAL SOURCE OF 986 MEN UNDERGOING VASECTOMY

Referral Source	No.	%
Family planning staff	487	49.4
Nonvasectomized man	255	25.9
Vasectomized man	82	8.3
Private physician	68	6.9
Other agency	50	5.1
Radio	21	2.1
Self or wife	6	0.6
Published material	5	0.5
Other	12	1.2

TABLE V
THE REASONS 986 MEN CHOSE STERILIZATION AS A METHOD OF CONTRACEPTION

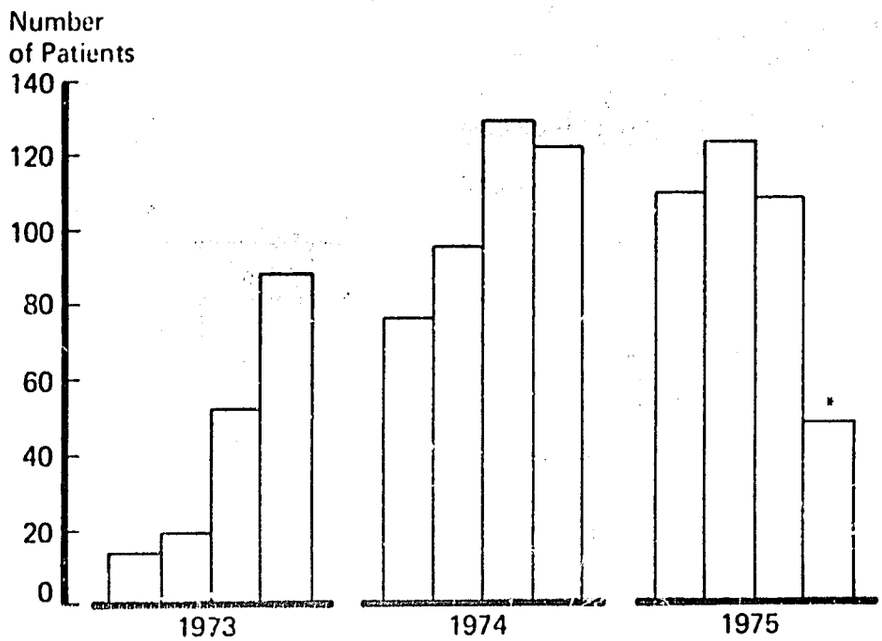
	No.	%
Other Methods		
Undesirable side effects	472	47.9
Inconvenient	39	4.0
Unavailable	1	0.1
Unreliable	2	0.2
Other reasons	472*	47.9

** Reasons given included, "Don't want any more children", "Economic problems", or "Health of wife".*

There was an increase in the rate (number/3 months) at which vasectomy was performed at the Asociación Pro-Bienestar de la Familia from 14 in early 1973 to 128 at its highest level in mid 1974. This level was maintained until late 1975 (Figure 1).

Very few problems were encountered at surgery (Table VI). Six men had complications: hematoma (3 men), testicular bleeding (1 man), and granuloma (2 men). One man complained of pain during the procedure.

All of the men in this study returned for a follow-up visit from 3 to 30 days after surgery. At the follow-up visit twenty-one men complained of mild (12 men), moderate (7 men), or severe (2 men) pain (Table VII). Table VIII shows the complications encountered 3 to 30 days after surgery. Thirty-four men (3.4%) had one or more complications at follow-up. The most frequent complications were scrotal abscess (1.2%), failure of the wound to heal (0.7%), and granuloma (0.5%). Most of the men (87.3%) had resumed intercourse by six days



** Patients for only one month.*

Figure 1. The Number of Patients Undergoing Vasectomy in Each Three-Month Period From 1973 Through 1975.

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TABLE VI
SURGICAL COMPLICATIONS FOR 986 MEN UNDERGOING VASECTOMY

	No.	%
Surgical Complications		
Hematoma	3	0.3
Bleeding from testis	1	0.1
Granuloma	2	0.2
Men with one or more complications	6	0.6

TABLE VII
PAIN AT FOLLOW-UP (3-30 Days After Sterilization) FOR 986 MEN UNDERGOING VASECTOMY

	No.	%
Pain at follow-up		
Mild	12	1.2
Moderate	7	0.7
Severe	2	0.2
Total	21	2.1

TABLE VIII
FOLLOW-UP COMPLICATIONS AT 3 TO 30 DAYS IN 986 MEN UNDERGOING VASECTOMY

Complication	No.	%
Abscess of scrotum	12	1.2
Wound not healed	7	0.7
Granuloma	5	0.5
Hematoma of scrotum	3	0.3
Scrotal swelling	2	0.2
Fever		
Not requiring antibiotics	1	0.1
Requiring antibiotics	1	0.1
Septic wound	1	0.1
Local skin infection	1	0.1
Men with one or more complications	33	3.3

after surgery (Table IX). Only 3.4 percent had not resumed intercourse at the follow-up visit. From the original population of 986 men, 525 men (53.2%) returned for a sperm test and examination more than 30 days after surgery. Most of these patients had no sperm (90.7%) and/or no motile sperm (98.9%) in the ejaculate (Table X), and none of the men had complications or complaints related to surgery.

TABLE IX
TIME TAKEN UNTIL RESUMPTION OF INTERCOURSE BY 986 MEN UNDERGOING VASECTOMY

Days	No.	%
0-3	71	7.2
4-6	790	80.1
7-9	53	5.4
10-15	7	0.7
16-20	1	0.2
Not resumed	36	3.4
Unknown	28	2.9

TABLE X
THE ASSESSMENT OF STERILITY IN 525 MEN WHO RETURNED FOR EXAMINATION AND A SPERM TEST AFTER VASECTOMY

	No.	%
Sperm presence		
No sperm present	476	90.7
1 or more sperm present	40	7.6
Unknown	9	1.5
Mobile sperm present		
No	519	98.9
Yes	6	1.1

IV. DISCUSSION

It is sometimes stated that vasectomy may not be acceptable to men in Latin America because of various cultural factors[4]. Chief among these factors is "machismo", a term describing the emphasis placed on overcompensating masculine traits in Latin America culture. When this concern for virility is combined with the ignorance and confusion surrounding vasectomy, it can readily be hypothesized that Latin American men might not readily accept sterilization. However, this report joins the growing body of literature[4,7,8] that indicates that when vasectomy and its effects are carefully explained, Latin Americans will undergo the procedure in large numbers. At the Asociación Pro-Bienestar de la Familia de Guatemala, almost 1000 men were vasectomized during a 34 month period, with the numbers per quarter increasing from 14 to 128. The patients

averaged only six years of education and fewer than 10 percent were professionals, thus refuting the theory that men in the upper socioeconomic classes would be the only ones who could be expected to accept sterilization.

In families where the desired family size has been reached, the parents must decide on an effective, acceptable contraceptive method to be used for a number of years. The contraceptive history in this population of men indicates that their wives had used oral contraceptives (63.4%) or an IUD (6.4%) for some time before they accepted vasectomy. Almost half (47.9%) of the patients stated that they had decided on vasectomy as the mode of contraception because these methods were associated with undesirable side effects. An additional 47.9 percent stated that they wanted no more children and had decided on vasectomy because it is a long term effective method of contraception, other than an IUD or oral contraceptives.

Information and advice about the various methods of contraception was obtained by the men in this study from friends, staff of family planning centers, and private physicians: 25.9 percent of the men were referred by men who had not been vasectomized, and 49.4 percent were referred by the staff of a family planning clinic.

Once a man learns about sterilization, acceptability becomes the second component in determining the frequency with which vasectomy is used as a long term method of contraception. In addition to the distribution of men having vasectomies over a specific period of time, acceptability was measured by the rate at which men were referred by vasectomized men, the time taken to resume intercourse, and the incidence of complications and complaints after the operation. There was an increase from 14 vasectomies per three-month period in 1973 to 128 per three months at its highest level in mid 1974. This rate was maintained until late 1975. This indicates that vasectomy was becoming more popular at the Asociación Pro-Bienestar de la Familia de Guatemala. While only 8.3 percent of the men in this study were referred by men who had had a vasectomy, this does not necessarily indicate that vasectomy is only moderately acceptable; it may simply reflect the small proportion of the male population in Guatemala who are vasectomized. The proportion of men giving this response could be expected to increase with time. There appeared to be no detrimental effects of vasectomy on libido, most men (87.3%) had resumed intercourse within a week of the opera-

tion and there were no complaints recorded by the 526 men returning for the first semen test. This is in agreement with psychological studies[2,4-6] which document few adverse sequellae of vasectomy. The data presented here on behavior and the absence of complications, variables which are more readily observable than attitudes, indicate that any concern about psychological or physiological sequellae to vasectomy may be unnecessarily exaggerated.

From data collected in this study of 986 men in Guatemala, it appears that in a population of men who were mostly skilled or unskilled workers, about 35 years old with a family size of four or fewer children and an educational attainment of 6.5 years, vasectomy is acceptable and free from complications and complaints.

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VASECTOMY AS AN OUTPATIENT PROCEDURE IN EL SALVADOR

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Abstract

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The experience of 200 men sterilized at the Asociación Demográfica Salvadoreña (ADS), a private outpatient family planning clinic, shows vasectomy to be a safe, effective method of permanent contraception, acceptable to many Salvadorian couples. Couples seeking male sterilization were better educated than those choosing female sterilization at the ADS, but they were less likely to have practiced contraception prior to sterilization. Over one third of the patients learned about the vasectomy program through other men who had been sterilized. Male sterilization has probably not been widely accepted in Latin America for the simple reason that it has not been offered.

I. INTRODUCTION

The enormous increase in family planning program activity that has occurred in Latin America since 1960 has been directed mainly at women. It was thought that the Latin male would leave family planning to the woman and would find male methods of fertility control, particularly sterilization, unacceptable (1). Recent experience has cast doubt on this assumption.

The first public male sterilization program in Latin America was started in Bogotá in February, 1970; since then, programs have been initiated in Costa Rica (1971), El Salvador (1972) and Guatemala (1973) (1). The Colombian experience has been so successful that the number of centers offering the procedure had to be increased. Male sterilization has probably not been accepted widely in Latin America for the simple reason that it has not been offered.

The Asociación Demográfica Salvadoreña (ADS), a private outpatient family planning clinic in San Salvador, El Salvador, offers male sterilization as an integral part of their patient services. The operations are performed by trained obstetricians and gynecologists rather than by urologists. This report summarizes the initial vasectomy experience at the ADS in an attempt to determine the feasibility of offering this procedure in a free-standing family planning clinic.

II. METHOD

From February, 1974, through November, 1975, 200 men underwent voluntary sterilization at the ADS. Socio-demographic and medical data were recorded on standard forms by the staff of the center. All patients were scheduled for follow-up examinations at eight days and six months after the sterilization in

addition to at least one semen test after the procedure.

III. RESULTS

Patient characteristics

Most of the men were married (92.5%) Roman Catholics (85.0%), who lived in the urban area of San Salvador (81.5%). Table I gives sociodemographic characteristics of the married patients and their wives. The mean age of the men sterilized was 34.3 years and their mean educational level was 7.1 years. Most of them were semi-skilled (35.5%) or unskilled (31.0%) workers.

The wives for whom data were collected were younger and less educated than the men in the study; the mean age of the wives was 28.7 years and they had completed a mean of 5.7 years of schooling. Most of the women (71.5%) were housewives.

Sociodemographic comparisons were made between those couples coming to ADS who selected female sterilization (725 during the same time period) and those who chose male sterilization. The age and employment status of the women were similar; mean age of female sterilization patients was 29.2 years and 66.1 percent were housewives. Educational attainment was higher for those couples selecting vasectomy as their means of permanent contraception. The female sterilization patients had a mean of 3.9 years of education, compared with 5.7 years for wives of men getting vasectomies. Men undergoing vasectomy had a mean education of 7.1 years, compared with 5.2 for the husbands of female sterilization patients.

Reproductive, Contraceptive, and Medical History

Reproductive data were collected on only half the men in the study. These men reported that they had fathered a mean of 4.6 children; a mean of 4.2 of these offspring were living at the time of sterilization (Table I). Women sterilized at ADS had a mean parity of 4.2.

Almost 10 percent of the men were being sterilized when they had only one or two living children; it is interesting to note that all of these children were female in 5 cases, all male in 3 cases and one of each sex in the other 11 cases, contrary to the expectation that Latin men would insist on male offspring before considering sterilization.

Forty-three percent of the men reported that they or their wives had not used a contraceptive method in the three months prior to sterilization; orals had been used by 26.5 percent of the couples, condoms by 14.5 percent, and IUDs by 7.5 percent. Two men reported that their wives had been sterilized. In contrast, only 2.3 percent of the women sterilized at ADS had not used a contraceptive prior to sterilization; 61 percent had used orals and 35 percent had used IUDs.

Motivation

Most of these men were referred to the ADS by other men who had been sterilized (37.0%) or by the family planning staff (19.5%). Only 13.0 percent listed themselves or their wives as the primary referral source. Half the men were asked why they had chosen sterilization over other family planning methods; 40.0 percent said that other methods were unreliable and 31.0 percent were concerned about the undesirable side-effects of the other methods.

Preexisting medical conditions were found for 17.5 percent of the patients; scrotal-testicular pain was the condition occurring most frequently (5.0%).

Clinic procedures

Each man who expressed interest in having a vasectomy was interviewed by a social worker. If the man chose to have the operation, he was assigned a time to return to the clinic. No pre-operative instructions were given to any of the men.

Before the patient was admitted to the operating room the scrotum was shaved and washed with soap and water. After the patient entered the operating room the scrotal area was prepared for surgery with an antiseptic solution. No pre-anesthetic medication was used.

In 88.0 percent of the procedures, 10 cc of 1% lidocaine was infiltrated into each side on the upper part of the scrotum, 2 cm below the inguinal ring. At each site the vas was identified, isolated, and grasped with an Allis forceps. A 1 cm vertical incision was made, the vas was isolated and dissected with a curved Murphy forceps, and hemostasis was performed. A simple ligation of the vas was made using chromic catgut "00", and a double ligation was used on the near end, folding it back on itself. The segment between the two points was removed. Hemostasis was confirmed and the incision was closed with two stitches of chromic catgut "00". The technique was the same for the additional 22.0 percent of the procedures except that these procedures were done through a single midline incision. The patient was then discharged to the recovery room where he remained for about two hours. The mean time taken to perform the operations was 16.3 minutes.

The patient was instructed to wait at least 24 hours before resuming his normal activities. Each patient was advised to use temporary contraceptives until sterility could be established by a negative semen test, usually performed after at least 15 ejaculations, or at the time of the three-month follow-up visit.

Complications and Complaints

There were no complications occurring during or immediately after surgery. Half the men were questioned about pain during the procedure; 14.0 percent reported mild pain.

At the time of the one-week follow-up visit, complications were recorded for 10.3 percent of the patients who returned for follow up and complaints were reported by 15.2 percent (Table II). The most frequently reported complication was wound infection (5.4%); none of the infections was severe enough to warrant treatment. Mild pain was reported by 12.5 percent of the men, moderate pain by 1.1 percent, and severe pain by 1.6 percent.

Nine tenths of the men returned for a follow-up visit one to six months after surgery. Of these, 1.7 percent reported complications and 2.8 percent reported complaints (Table III).

Failures and Potential Failures

No pregnancies had been reported at the time of analysis, over a year after the last study procedure was performed.

Semen tests were performed on 136 of the men returning for the one-to six-month follow-up. For this analysis, men having positive semen tests were

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considered potential method failures. Semen tests were positive (gave evidence of live or dead sperm) for four (2.9%) of these men. Two never returned for a second semen test; the semen tests for the other two men six months after surgery were positive. The results for these men are not entirely conclusive, since a one-year follow-up test may have been negative or their sperm counts may have been too low to impregnate.

IV. DISCUSSION

This analysis shows vasectomy to be a safe, relatively effective method of permanent male contraception, acceptable to many of the Salvadorian couples coming to the ADS for sterilization. The complication rates were low, except for mild incision infection noted at the one-week follow-up visit; although this might be a complication of any operation, efforts should be made to minimize it. Almost all of the pain experienced by the patients was reported as mild and easily relieved by analgesics. The potential failure rate was lower than that reported for another Latin American study (2).

Although the couples seeking male sterilization were better educated than those choosing female sterilization, they were less likely to have practiced contraception before sterilization. Presser (3) found similar educational differences in a study of Puerto Rican couples, but her data showed no difference in contraceptive use.

Over one third of the men learned about the ADS vasectomy program through other men who had been sterilized. Those previously vasectomized men who recommended the ADS seem to have been satisfied with their experience.

A group discussion was held by 45 farm laborers sterilized at the ADS since its inception in 1972 (4). The opinions and examples of the union leaders and the economic pressure of many children on a family with limited resources influenced the men to seek sterilization. The men expressed satisfaction with the procedure, saying that their sexual relations were improved and more enjoyable now that there was no worry about pregnancies. Although postoperative pain was experienced by some of the men, most of the operations were free from complications and complaints.

Vasectomy has only recently been offered in Latin American countries. Misconceptions about its unacceptability in "male-dominated" cultures have been challenged by its increasing popularity in those countries where it is offered.

Table I

SELECTED SOCIO-DEMOGRAPHIC CHARACTERISTICS OF 200 MEN UNDERGOING VASECTOMY AT THE UNIVERSIDAD de EL SALVADOR, FEBRUARY, 1974-NOVEMBER 1975 AND THEIR WIVES

	Patients (N=200)		Wives (N=183)	
Age				
<30	54	27.0	112	61.2
30-34	62	31.0	39	21.3
35-39	37	18.5	20	10.9
40+	46	23.0	12	6.6
Unspecified	1	0.5	0	0.0
Mean	34.3		28.7	
Education				
None	12	6.0	17	9.3
1-6	102	51.0	114	62.3
7-12	68	34.0	48	26.2
13+	18	9.0	4	2.2
Mean	7.1		5.7	
Occupation				
Professional	26	13.0	15	8.2
Manager/proprietor/farm owner	17	8.5	1	0.5
Clerical	5	2.5	3	1.6
Craftsman	8	4.0	4	2.2
Operative	71	35.5	5	2.7
Laborer/farm worker	62	31.0	9	4.9
Other	3	1.5	9	4.9
Unemployed	3	1.5	131	71.5
Unspecified	5	2.5	6	3.3
Marital Status				
Married, one wife	183	91.5		
Married, more than once	2	1.0		
Formerly married	15	7.5		
Children fathered				
1-2	16	8.0		
3-4	41	20.5		
5-6	26	13.0		
7+	17	8.5		
Unspecified	100	50.0		
Mean	4.6			

Table II

COMPLICATIONS AND COMPLAINTS OF 200 MEN UNDERGOING VASECTOMY AT THE UNIVERSIDAD de EL SALVADOR, FEBRUARY 1974-NOVEMBER 1975

Early (one week) Follow-up Complications (N=184)	No.	%
Wound septic	10	5.4
Scrotal hematoma	3	1.6
Hydrocele	1	0.5
Granuloma	2	1.1
Local skin infection	1	0.5
Herpes Zoster (gland)	1	0.5
Bleeding at first intercourse	1	0.5
Total Men With Early Follow-up Complications	19	10.3
Early Follow-up Complaints (N=184)		
Mild pain	23	12.5
Moderate pain	2	1.1
Severe pain	3	1.6
Total Men With Early Follow-up Complaints	28	15.2
Late (one to six months) Follow-up Complications (N=180)		
Granuloma	1	0.6
Pain in testes	1	0.6
Acute lumbar pain (probably work related)	1	0.6
Total Men With Late Follow-up Complications	3	1.7
Late Follow-up Complaints (N=180)		
Lessened sexual activity	2	1.1
Diminished ejaculation fluid	1	0.6
Impotency (treated before surgery)	2	1.1
Total Men With Late Follow-up Complaints	5	2.8

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POSTABORTION INSERTIONS OF THE PLEATED MEMBRANE

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ABSTRACT

Tacla, X., Mitra, M. and Baeza, R. (Barros Luco Hospital, Santiago, Chile, and International Fertility Research Program, Research Triangle Park, North Carolina, USA). Postabortion Insertions of the Pleated Membrane.
Int J Gynaecol Obstet

The pleated or intrauterine membrane (IUM) was designed to fit a range of uterine sizes and shapes and to adjust to transient changes resulting from uterine motility. The retention and contraceptive abilities of postabortion IUM insertions are analyzed in this study of 154 IUM insertions made within 3 days of treatment for an incomplete or inevitable abortion.

Results indicate low 1-year net cumulative event rates for pregnancy (1.7 per 100 users), expulsion (7.2 per 100 users), and removal for bleeding and/or pain (3.9 per 100 users). These rates were similar to those reported in a study of interval insertions of the IUM; moreover, these results also compared favorably with corresponding rates of postabortion insertions reported in studies using other devices. Thus, the postabortion period is indicated as being an effective time for IUM insertion.

INTRODUCTION

This study evaluates 154 insertions of pleated membrane intrauterine devices (IUDs) in patients treated for spontaneous or incomplete induced abortions at the Barros Luco Hospital, Santiago, Chile, between May 1974 and March 1976. The patients were all inserted with an intrauterine membrane (IUM) before discharge from the hospital and within 3 days of undergoing dilatation and curettage (D&C) for an incomplete or inevitable abortion.

Previous experience has shown that a birth control program focused on women who have terminated an unwanted pregnancy is likely to be more effective than a general program for all fertile women (10). Moreover, initiating contraceptive protection prior to hospital discharge has been shown to contribute to a better family planning program than a program which depends on the patients to return for services.

Studies conducted with different kinds of IUDs inserted immediately after an abortion have shown that the postabortion period is a favorable time for IUD insertion (1, 4, 5). However, postabortion experiences may be varied, depending upon the individual IUD design. Moreover, since the structure of the postabortion uterus is different from that of the postmenses uterus (i.e., the postabortion uterus is more likely to be larger and more subject to uterine contractions), experiences with interval insertions of a particular device may not be duplicated in a postabortion IUD program using the same device.

One of the distinctive features of the pleated membrane IUD is its horizontal compliance, which is designed to absorb uterine contractions (6). This study reports the results of the first trial of postabortion insertions of the pleated membrane. These results are compared with those of interval insertions of the same device* and with those of postabortion insertions of other devices.

MATERIALS AND METHODS

The device

The IUM, which is made from Alathon-20 polythene, has a large surface area (2 350 mm^2) (Fig. 1). Its ability to fit different sized and shaped uteri and to adjust to uterine motility results from its corrugated structure, its thinness (0.0005 mm), and the flexibility of Alathon-20 polythene. A barium-sulphate injection molding strengthens the base of the device. The IUM is seated in the flat funnel-shaped base of the insertion tube and is pulled into the tube proper by a string. The device is moved to the distal end of the insertion tube by a pushrod. The tube is then entered into the uterus and the IUM inserted by withdrawing the outer tube, while holding the inner pushrod steady.

Acceptor characteristics

The age and parity means of the women were 27.2 years and 2.3 live births (Table I). Many (41.6%) reported no previous contraceptive practice. The most commonly reported forms of contraception used by the

*Early trials of interval insertions of the pleated membrane have shown that the device combines low pregnancy and expulsion rates with high bleeding/pain removal rates (7).

women were IUDs (33.8%) and oral contraceptives (18.2%). For more than half of the women (64.3%), this abortion was the first; the remainder (35.6%) had had more than 1 abortion.

All of the 154 women in the study had the IUM inserted within 3 days of undergoing a D&C for treatment of an inevitable or incomplete abortion (Table II). Each woman was required to return for follow-up visits at 1, 3, 6, and 12 months after the IUD insertion.

Methodology

Life-table rates for various events, computed by the Tietze Method (8), were used to evaluate the performance of the IUM device for post-abortion users. The cutoff date for the study was set at April 1, 1976.

RESULTS

At the end of 1 year of IUM use, the net cumulative continuation rate was 77.7 per 100 users. At 1 year, less than 10% of the cases were lost to follow-up.

Pregnancy

The 1-year net cumulative pregnancy rate was 1.7 per 100 users (Table III). Five women became pregnant during the study period. Two women were continuing their pregnancies at their last follow-up visits; 2 terminated their pregnancies--1 by inducing menses and another by an induced abortion. The fifth woman had a spontaneous abortion. Four of the 5 women who became pregnant were determined to have had the IUM *in situ* at conception.

Expulsion

The 1-year net cumulative expulsion rate was 7.2 per 100 users. Ten women expelled the IUM during the study. Most expulsions occurred early in the study; the mean time from insertion to expulsion was 4.6 months. Expulsions were also most frequent among those who had the IUM inserted on the day after the abortion procedure (Table II).

Bleeding and/or pain removal

The 1-year net cumulative bleeding and/or pain removal rate was 3.9 per 100 users (Table III). Two women had the IUM removed for bleeding and/or pain. One complained of severe menorrhagia and had to be treated as an emergency case, and the other complained primarily of pain.

Removals for other medical reasons

The 1-year net cumulative rate of removals for other medical reasons was 5.5 per 100 users (Table III). Several (7/11) of the complaints and consequent removals for other medical reasons were made within 6 months of the abortion and IUM insertion. Pelvic inflammatory disease was the primary reason for the 11 removals. Four women had to be hospitalized for treatment of infection, and 1 other was treated for infection as an emergency case. Although several complaints of infection were reported and at least 4 women were hospitalized for infection, it was not determined whether this reflected the incidence of infection in the population or whether it was associated with the IUMs or with the category of patients using IUMs.

DISCUSSION

The results of this study indicate that postabortion insertion of the IUM is safe and effective. Seventy-eight percent of the women in this study were still continuing use of this device 1 year after insertion. One-year pregnancy, expulsion, and bleeding/pain removal rates were 1.7, 7.2, and 3.9, respectively, per 100 users. At the end of 1 year, there were 5.5 removals per 100 users for all other medical reasons.

During this study, 4 women were hospitalized for infection. However, this rate of rehospitalization is not higher than would be expected in a noncontracepting group of women treated for completion of an illegally induced abortion.

Pregnancy, expulsion, and bleeding/pain removal rates derived from this study of postabortion IUM insertions compared favorably to similar rates derived from a preliminary study of interval IUM insertions (7) and to results from studies of postabortion insertions using other devices (Tables IV and V).

Previous experiences comparing postabortion with postmenses insertions of IUDs show no consistent relationship with expulsion rates. This inconsistency may be due to the interaction of several factors, including differences in acceptor groups, inserter skills, and the devices themselves.

The possibility of IUD insertion causing increased complications during the patient's postoperative period is a major concern. In this

study, 4 women were rehospitalized after IUM insertion in the post-abortion period. Previous studies in which an IUD was inserted immediately after completion of an elective first trimester abortion indicate that there is no apparent increased risk for those accepting an IUD than for those who do not (9). Goldsmith and his co-workers reported no significant differences in postoperative complications between women who accepted or did not accept IUDs immediately after undergoing an illegal or spontaneous abortion (4). No information concerning rehospitalization was noted. In another study of elective abortions, no significant differences were noted between the control and the IUD acceptor groups in terms of rehospitalization (9). In that study, the rehospitalization rate for those accepting an IUD was 1.3 per 100 women, and the corresponding rate for non-acceptors was 3.5.

The risk of perforation resulting from postabortion IUD insertions is another important concern. However, there were no perforations in this study, and other studies cited in this paper (2) have also found low perforation rates resulting from postabortion IUD insertion.

The fact that many of the women in this study chose to terminate their pregnancies by illegal means places a burden on the physician to minimize the potential for future abortions. Whereas the risk of infection and expulsion is still a major concern for women who undergo IUD insertion immediately after completion of an illegal abortion, it should be noted that, compared to the relative risk of complications from another illegal abortion, the risk of complications resulting from IUD insertion is small. In the context of similar studies, this study

indicates that postabortion IUD insertion is an optimal time to provide IUD contraception.

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TITLES AND LEGENDS

Tables I - V: Titles on tables.

Figure 1: Title: Standard pleated membrane intrauterine device.

Legend: None.

TABLE I

SELECTED SOCIO-DEMOGRAPHIC AND REPRODUCTIVE CHARACTERISTICS OF 154 WOMEN INSERTED WITH THE STANDARD IUM, BARROS LUCO HOSPITAL, SANTIAGO, CHILE, MAY 1974 – MARCH 1976

Characteristics	No.	%	Characteristics	No.	%
Age			**Total Abortions**		
Less than 20	16	10.4	1	99	64.3
20–24	48	31.2	2	33	21.4
25–29	38	24.7	3	12	7.8
30–34	27	17.5	4 or more	10	6.4
35–39	19	12.3			
40 or more	6	3.9	**Contraceptive Practice Before This Procedure**		
Mean	27.2				
Parity					
0	15	9.7	None	64	41.6
1	41	26.6	Condom	1	0.6
2	41	26.6	Diaphragm/foam/jelly	1	0.6
4	31	20.1	IUD	52	33.8
5 or more	26	16.8	Orals	28	18.2
Mean	2.3		Other	8	5.2

TABLE II

NUMBER AND PERCENTAGE OF INSERTIONS AND EXPULSIONS BY POSTABORTION DAY OF INSERTION FOR 154 WOMEN INSERTED WITH THE IUM, BARROS LUCO HOSPITAL, SANTIAGO, CHILE, MAY 1974 – MARCH 1976

Days Post-abortion	Insertions		Expulsions	
	No.	%	No.	%
0	4	2.6	0	0.0
1	89	57.8	9	5.8
2	46	29.9	1	0.6
3	15	9.7	0	0.0
Total	**154**	**100.0**	**10**	**6.4**

TABLE III

ONE-YEAR NET CUMULATIVE EVENT RATES FOR 154 WOMEN INSERTED WITH THE STANDARD IUM BETWEEN MAY 1974 AND MARCH 1976

Event	Rates
Pregnancy	1.7 ± 1.2*
Expulsion	7.2 ± 2.2
Removals	
Bleeding and/or pain	3.9 ± 1.7
Other medical reasons	5.5 ± 1.9
Planned pregnancy	0.8 ± 0.8
Other personal reasons	3.2 ± 1.6
Cumulative continuation	77.7
Lost to follow-up	7.7
Cutoff date	April 1976

* *Standard deviation.*

TABLE IV
NET CUMULATIVE ONE-YEAR EVENT RATES OF POSTABORTION IUD INSERTION STUDIES

Study	Type of Device	No. of Insertions	Pregnancy	Expulsion	Bleeding/ Pain Removals	Perforation
Boria(2)	Lippes Loop	422	3.2	17.2	–	1/422
Faundes(3)	Lippes Loop	705	2.9	16.5	4.5	
Andolsek(1)	Lippes D	664	2.0	2.8	2.9	
Faundes(3)	Cu-T 200	639	3.5	13.0	1.8	
Timonen(9)	Cu-T 200	154	3.3	0.0	–	

TABLE V

SELECTED NET CUMULATIVE SIX-MONTH EVENT RATES OF POSTABORTION AND INTERVAL INSERTIONS OF THE IUM

	Interval	Postabortion
Pregnancy	1.1	0.0
Expulsion	5.9	5.5
Removals		
Bleeding and/or pain	9.6	2.1
Other medical reasons	3.3	4.7

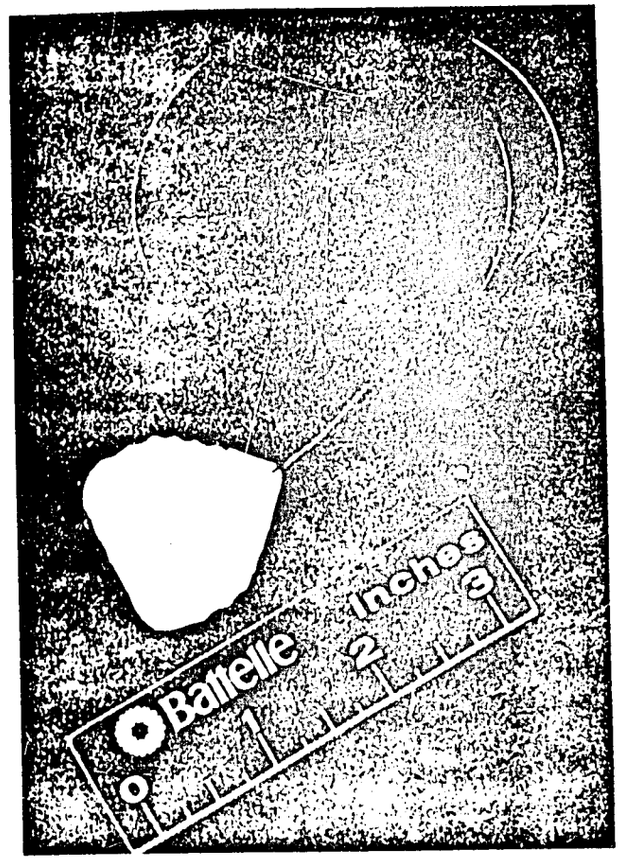

Fig. 1. Standard pleated membrane intrauterine device.

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IUD 43
OR

ELECTROCHEMICAL EFFECTS OF METALS ON IUDs

By

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Abstract

Zipper, J. (Dept. Biophysics and Physiology, School of Medicine, Univ. Chile, Santiago, Chile), Wheeler, R. G. (Staff Engineer, Int. Fertility Research Program, Research Triangle Park, North Carolina), Adrian, H. (Dept. Biophysics and Physiology, School of Medicine, Univ. Chile, Santiago, Chile), and Angelo, S. (Dept. Biophysics and Physiology, School of Medicine, Univ. Chile, Santiago, Chile). *Electrochemical Effects of Metals on IUDs... Int J Fertil*
Electrochemical effects within the uterus are being studied, particularly as they pertain to IUDs made in total or in part of metals.

The intrauterine potential as measured with either metal or nonpolarizable salt electrodes is positive at the fundal with respect to the cervical end of the uterus. Placement of dissimilar metal electrodes within the uterus will induce voltage gradients that are roughly predictable from their cell potential in blood as an electrolite. When copper and zinc electrodes are placed at opposite ends of the uterus, they induce voltage gradients that are typically greater than 100 mv per cm. External copper and zinc wires connected at one end and with the other ends in contact with various positions on the skin of rats were found to influence potential gradients within the uterus.

When a length of zinc wire was wound around the upper portion of the stem of a small Cu-7 200 IUD, it took about one year from insertion for the zinc to disappear. When the zinc wire was wound around the lower portion of the stem, it disappeared in one month. The zinc reduced intrauterine corrosion of the copper and it was more effective at reducing copper corrosion when in the lower stem position.

INTRODUCTION

The authors have investigated some of the characteristics of metals on IUDs that are due to the electrical cell formed by ionic concentration gradients in the uterine fluid or by dissimilar metals. The voltage of a cell may be demonstrated simply by placing one end of two wires made of different metals into an electrolite and connecting the other two ends to a voltage or current measuring instrument. A negative charge will build up on the metal with the highest solution pressure in the electrolite as its atoms convert to cations. Current will flow through the measuring instrument from the positively to the negatively charged electrodes.

In the experiments to be described, using animal and human subjects, we have measured intrauterine potentials with both polarizable and non polarizable electrodes, and the cell potential of two different metal electrodes placed within the uterus. We have observed the effect on intrauterine potentials of an external voltage applied to body skin by a cell made of different metals and the effect on IUD event rates produced by placing zinc and copper in different positions on an IUD.

MATERIALS AND METHODS

Metal electrodes were made of chemically pure metal wires 0.5 mm in diameter and insulated except for 2 mm at the end for rats and 1 cm for women. Non-polarizable electrodes were made of 3 molar KCl in 2% agar inside polyethylene tubes 0.85 mm I.D. and 1.25 mm O.D. This KCl electrode is connected through a

3M KCl solution to an Ag wire anodized in HCl. Fresh electrodes were prepared for each determination and the systems were checked for polarization in heparinized rat blood and KCl solution before use.

Rats in proestro were the experimental animals. Electrodes were introduced through small holes made in the superior and inferior portion of the uterus. Electrode contact with the skin of the rats was made by shaving and cleaning the skin and adding a drop of physiological saline to reduce the contact resistance. Voltage measurements were obtained with a Tektronix 502 dual beam oscilloscope. Cu-7 IUDs were used to position Zn and Cu electrodes within the uterine cavity of the women subjects. In one series, a portion (1 cm) at the end of the Zn and Cu electrodes was stripped of insulation. The uninsulated wire ends were wrapped around either the superior or inferior portion of a plain 7 IUD stem so that the electrodes were 3 cm apart. Intrauterine electrode voltage in woman subjects was measured during the proliferative stage of the menstrual cycle.

For IUD studies on the effect of sustained intrauterine exposure to dissimilar metals, 47 mm^2 surface of Zn was placed either at the superior stem position or inferior stem position on a standard Cu-7 IUD by winding 0.56 mm diameter pure Zn wire around the stem. After various time intervals up to 13 months, the IUDs were removed and assays were made to determine the amount of Zn and Cu loss. Total Zn remaining was assayed. The difference between the original weight and the weight of the Zn remaining was recorded as the amount lost. The amount of copper present on the wire as cuprous oxide was determined by first dissolving the oxide in 6N HCl at room temperature and then subjecting it to atomic absorption spectroscopic analysis. The undissolved dry wire was then weighed. Thus, copper loss is equal to the initial amount of Cu minus Cu in the oxide film minus Cu remaining after HCl treatment.

RESULTS

Results are presented here as a series of electromotive force measurements on both human and animal subjects. These measurements are used to interpret clinical data in which both copper and zinc are present on Cu-Zn-7 IUDs.

Intrauterine Potentials

Intrauterine potentials in rats were measured with Ag-AgCl-(Agar KCl) electrodes. The superior electrode was directed downward and located 5 mm from the utero-tubal junction. The inferior electrode was also directed downward and was inserted 1 cm from the utero-cervical junction. Measurements were also made with Cu-Cu and Ag-Ag electrodes positioned the same way. The cell outputs were observed one to two minutes. Voltages obtained with the three types of intrauterine electrodes are listed in Table I.

Uniformity of the intrauterine voltage gradient in each of the animals was measured with the (Agar-KCl) electrodes by reversing the tip direction of the lower electrode and slowly reducing the electrode separation by advancing the lower toward the superior electrode. In each case the voltage decreased linearly with decrease in separation, and the polarity reversed when the moving electrode passed the superior electrode.

Measurements on nine women made with Cu-Cu electrodes 3 cm apart on a Cu-7 IUD are listed in Table II. Similar measurements in women subjects were made with the Ag-AgCl-(Agar-KCl) electrodes. The two electrode tubes were joined so the spacing between them was 2.5 cm. The measurements taken immediately after insertion of the electrodes are presented in Table III.

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Intrauterine Cell Voltage

Intrauterine electrode voltages were measured on cells consisting of Cu and Zn electrodes positioned in seven rat uteri as previously described. In all cases the Zn was negative about 450 mv. Changing the position of the electrodes did not noticeably affect the cell output. The same voltage was obtained with heparanized rat blood as the electrolite. The large output of this cell masked any differences in voltage produced by reversing electrode positions within the uterus.

Similar intrauterine measurements with Cu-Zn electrodes were made on two women subjects. By alternating the position of the Cu and Zn electrodes, four readings were obtained. In all cases, the cell potential at the Zn electrode was -700 mv.

Electrodermal Effects on Cell Potentials

A copper electrode in one uterine horn of a rat was connected successively to seven different metal electrodes in contact with the abdominal skin of the rat. The experiment replicated in seven rats produced the results listed in Table IV.

No electrodermal-potential experiments were done with women subjects; however, the voltage between a Cu electrode at the fundus and the stainless steel speculum positioned in the vagina was measured in seven women. The average voltage measured at the Cu electrode was -363 mv. The minimum was -400 and the maximum was -300 mv.

Voltage measurements were made with Ag wire electrodes introduced into the superior and inferior portions of one horn of the rat uterus as described

previously. Zn & Cu wire electrodes joined at one end were connected to the abdominal skin of the rats so that one electrode was below the uterus and the other above. The effect of the Cu-Zn cell potential on the Ag-Ag electrodes in the uterus was measured with the Cu electrode in the superior and the Zn electrode in the inferior positions. Measurements were also made with the Cu and Zn electrodes reversed. Each time the skin electrodes were connected or disconnected, transient polarization was evident on the cathode ray tube as illustrated in Figure 1. The effect of the electrical field of the Cu-Zn cell on the output of the intrauterine Ag-Ag electrodes is presented for nine animals in Table V. Notice in Figure 1 and Table V that the fundal Ag electrode is normally positive. When the external cell is connected with the Cu in the superior position, the polarity of the intrauterine cell is reversed. When the Zn electrode is in the superior position, the fundal Ag electrode becomes even more positive with respect to the cervical electrode.

Copper-Zinc IUDs, Cu-Zn-7

We wished to determine if over a period of time the intrauterine concentration gradients and potential gradients would influence metal corrosion rates. The intrauterine potential gradients are much less than the potential of the intrauterine Zn-Cu cell which also exceeds any myoelectric or electrodermal potentials (1). Over a prolonged period, however, the intrauterine gradients could accelerate corrosion rates if they have the same polarity as the Zn-Cu cell and retard corrosion if the gradient is in opposition to the Zn-Cu cell potential. Copper and Zn weight loss for intrauterine exposures up to 13 months are listed in Table VI. The initial weights of the 200 mm^2 surface Cu wire and the 47 mm^2 surface Zn wire were 89 and 31.4 mg, respectively.

2.4d

DISCUSSION

Results of voltage measurements on biological systems depend so much on equipment and technique that there is little consistency in the reports on intrauterine potentials. For example, Feo (2) reports that in 22 out of 30 measurements of pH, the fundal portion was more basic by as much as 0.6 pH units than the cervical portion. Yedwab et al (3), on the other hand, found in 40 women an average pH difference of only 0.01 pH units between the cervical and fundal portions of the uterus. Their pH cells had long time constants so the instantaneous pH difference between the fundal and cervical portions could be larger than the reported average. They did find the oxygen pressure during the ovulatory phase to be about 90 percent greater in the cervix than at the fundus. The average potential gradient of 2.1 mv/cm from fundus to cervix in the seven women subjects of this study is consistent with the intrauterine zinc and copper corrosion results. A higher oxygen pressure in the cervix region could also account for greater corrosion of metals in the cervical portions of IUDs than in the fundal portion.

Polarizable metallic electrodes in both women subjects in the proliferative phase of the menstrual cycle and rats in proestro produced fundus to cervix potential gradients greater than those observed with the Ag-AgCl-(Agar KCl) electrode. On the average these gradients for copper electrodes were 18 mv/cm in women and 14 mv/cm in rats. Independent of its acting as a source of copper ions, a copper IUD would alter the chemistry of the uterus by virtue of the potential gradient it creates. We would expect an IUD in which the copper elements are physically separated as in the Cu-Loop and TCu 220C to have a

different electrochemical effect on the uterus from one in which the copper element is continuous, as in the Cu-7 and Cu-T 200 (4).

The reproduceable reversal of polarity and polarization transients of Ag-Ag intrauterine electrodes in rats produced by the reversal of external voltage from a Cu-Zn-skin cell suggests the possibility of altering reproductive function with an external cell or applied potential.

We know from the work of Zipper et al. (5) that on the average no less than half of the 90 mg of copper originally on the Cu-7 remains after four years of use. The initial rate of release of Cu is reported from several sources (4, 6, 7) to be about 60 μg/day. Assuming the amount of copper lost with time fits the relationship:

$$w = 90 - ae^{bt}$$

where w is the amount of copper lost in mg and t is days since insertion, the constants a and b can be evaluated. Substituting 90 mg for w when t=0 and 45 for w when t=1460 days (4 years) provides the following approximate model for copper released:

$$w = 90 - 90\ e^{-.000475t}$$

This copper loss from the Cu-7 IUD as a function of days since insertion is plotted in Figure 2. Copper loss from the four Cu-Zn IUDs with zinc in the superior position are also plotted Figure 2. Since all the points fall below the curve for plain Cu-7 IUDs, it appears that zinc in the superior position has reduced the copper corrosion rates slightly by acting as a sacrifical anode.

The measured copper loss on the Cu-Zn 7 IUDs with the zinc in the inferior position is plotted in Figure 3. Since the IUD removed after one month is the only one with any zinc remaining, and since all the points fall far below the standard Cu-7 curve, it looks as if zinc in the inferior position completely supresses copper corrosion as long as the zinc lasts. There seems to be some residual copper protection even after the zinc is gone.

The role of zinc added to a copper IUD in improving contraceptive efficacy has been established (8, 9, 10, 11). Preliminary evidence indicates the placement of the zinc, hence the polarity of the IUD, influences expulsion rates (12). According to in vitro and animal studies, the motility of uterine smooth muscles varies inversely with the concentration of Cu ions (13, 14). The effects of IUD polarity on IUD expulsion have not been separated experimentally from Cu ion concentration effects. Larger and more definitive studies will be required to ascertain the effect of voltage gradients in the uterus on IUD event rates and to separate copper ion effects per se from electrolytic effects.

TABLE I

INTRAUTERINE VOLTAGES IN RATS

Ag–AgCl (Agar–KCl) Superior Electrode (MV)			Cu–Cu Superior Electrode (MV)			Ag–Ag Superior Electrode (MV)	
Animal	Horn 1	Horn 2	Animal	Horn 1	Horn 2	Animal	Horn 1
1	0	+10	11	+30	+20	16	+1
2	+3	+15	12	+90	-50	17	+4
3	+5	+5	13	-50	+40	18	+5
4	+5	+5	14	+50	+20	19	+5
5	+20	+10	15	+30	+30	20	0
6	+10	+15				21	-4
7	+15	+15				22	+8
8	+5	+15				23	+6
9	+10	+2.5				24	0
10	+10	+2					

TABLE II

INTRAUTERINE VOLTAGES IN WOMEN WITH Cu WIRE ELECTRODES SPACED 3 cm APART ON VERTICAL STEM OF Cu–7 IUD ELECTRODE SUPPORT

Subject	Superior Electrode (MV)	Subject	Superior Electrode (MV)
1	+100	6	+30
2	+100	7	+20
3	+100	8	-20
4	+100	9	0
5	+50		

TABLE III

INTRAUTERINE VOLTAGES IN WOMEN WITH Ag–AgCl–(Agar KCl) ELECTRODES SPACED 2.5 cm APART ALONG UTERINE AXIS

Subject	Superior Electrode (MV)	Subject	Superior Electrode (MV)
1	+4.5	5	+5
2	+5.0	6	+10
3	+5.0	7	+5
4	+2.0		

TABLE IV

VOLTAGE OF INTRAUTERINE CU ELECTRODE AND ELECTRODES ON THE ABDOMINAL SKIN OF RATS

Skin Electrode Material	Skin Electrode Potential (MV) by Animal						
	1	2	3	4	5	6	7
Cu	+50	+50	+40	+60	+30	+50	+40
Au	+50	+20	+20	+20	+10	+45	+30
Ag	+220	+200	+200	+200	+200	+100	+100
Co	-50	-20	-80	-70	-80	-100	-100
Pb	-150	-100	-170	-100	-200	-150	-130
Cd	-300	-280	-360	-300	-380	-300	-340
Zn	-500	-500	-600	-500	-580	-450	-500

TABLE V

THE EFFECT OF THE ELECTRICAL FIELD PRODUCED BY Cu & Zn CONNECTED IN SERIES WITH THE RAT ABDOMEN ON THE VOLTAGE OF Ag–Ag ELECTRODES IN THE RAT UTERUS

	Superior Electrode Potential of Ag–Ag Intrauterine Electrodes*				
Animal	Ag–Ag Only (MV)	Cu Superior Zn Inferior	Induced Change	Zn Superior Cu Inferior	Induced Change
1	+1	-1	-2	+2	+1
2	+4	+2	-2	+5	+1
3	+5	+3	-2	+6	+1
4	+5	0	-5	+7.5	2.5
5	0	-2	-2	+2	+2
6	-4	-9	-5	+2	+6
7	+8	-2	-10	+10	+2
8	+6	-2	-8	+2	+8
9	0	-3	-3	+3	+3

** Skin electrode positions values are (MV).*

TABLE VI

Cu AND Zn LOSS FROM Cu–Zn–7 IUDS WITH THE Zn IN EITHER THE SUPERIOR (s) OR INFERIOR (i) STEM POSITION

Woman Subject	Zn Position	Esposure (Months)	Zn Loss (mg)	Cu Loss (mg)
1	s	6	2.3	5.6
2	s	11	23.7	6.0
3	s	13	31.4*	12.6
4	s	13	9.4	6.9
5	i	1	29.6	0.1
6	i	3	31.4*	0.7
7	i	4	31.4*	0.8
8	i	9	31.4*	0
9	i	12	31.4*	5.7

* *Zn was gone.*

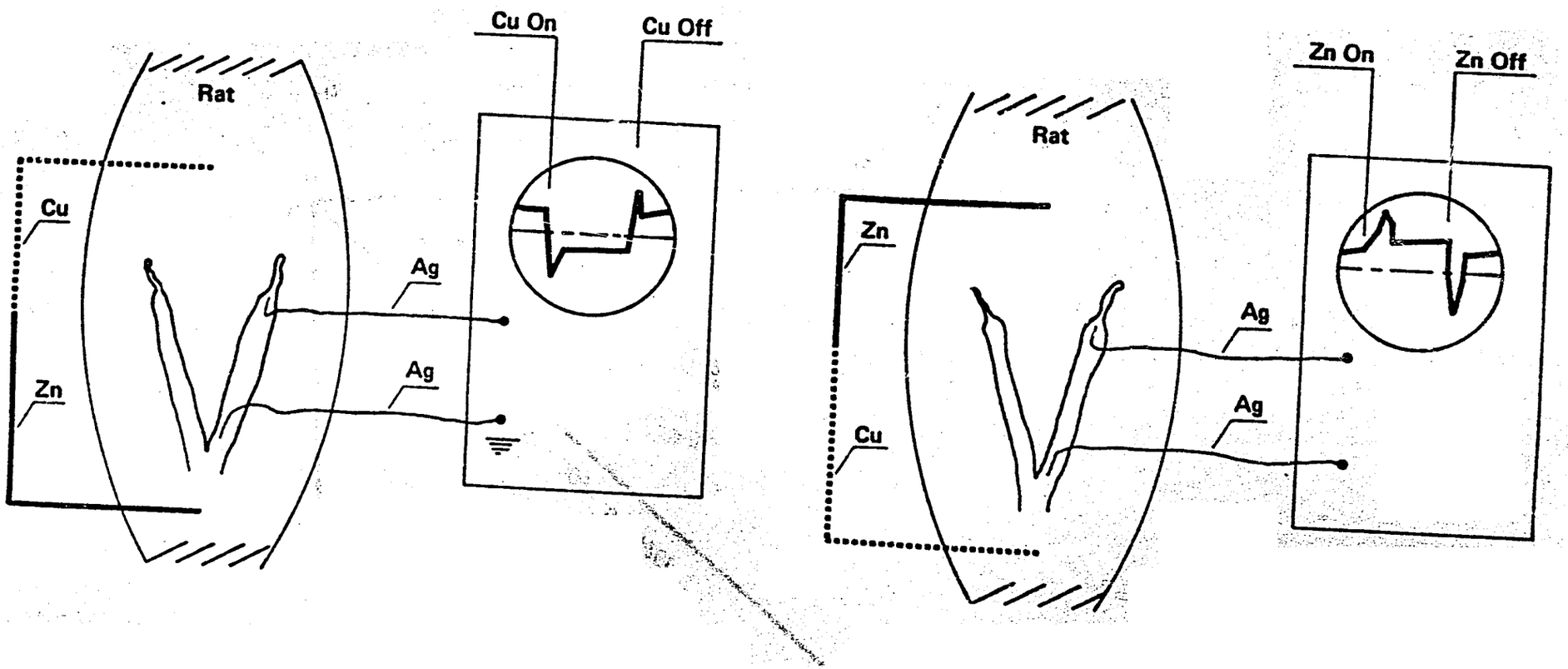

Figure 1. The Effect of an External Potential on Intrauterine Potentials.

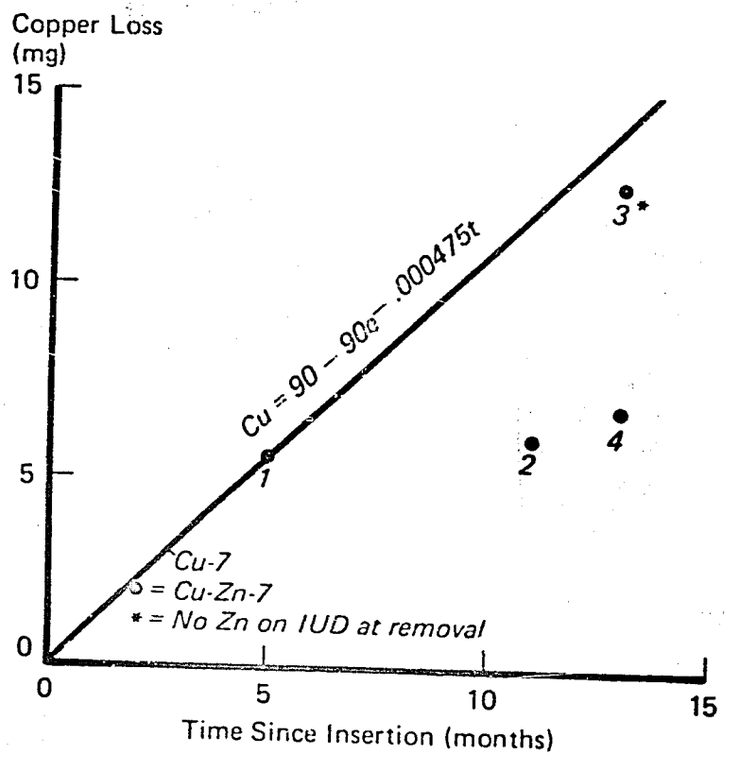

Figure 2. Copper Loss From Cu-7 and Cu-Zn-7 (Zn Superior Position).

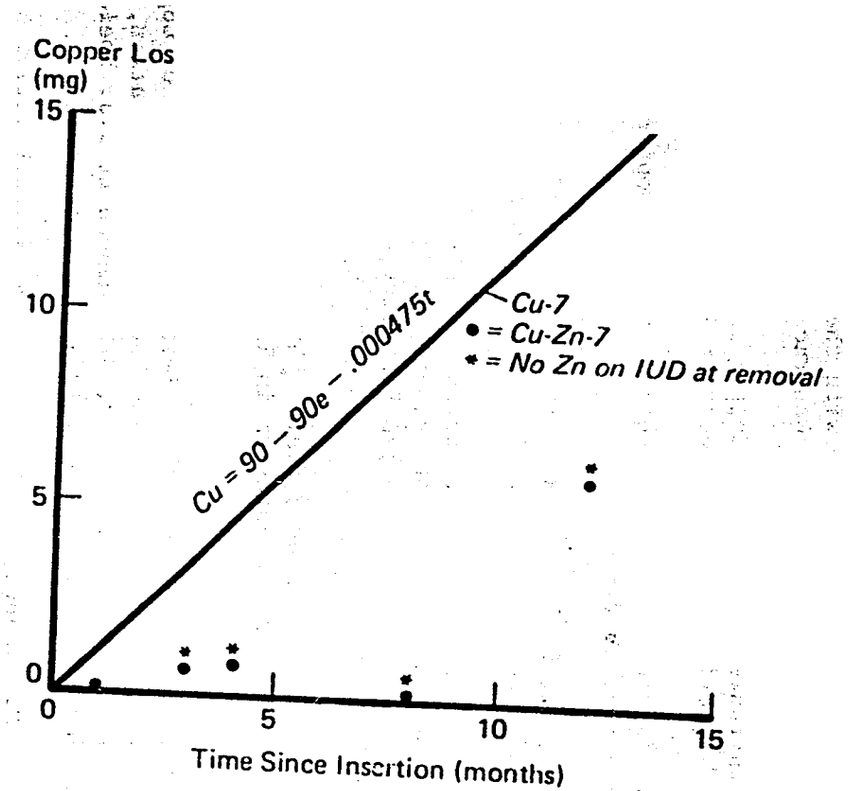

Figure 3. Copper Loss From Cu-7 and Cu-Zn-7 (Zn Inferior Position).

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An Overview of IUD Research and Implications for the Future

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ABSTRACT

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The limitations of nonmedicated intrauterine devices (IUDs) and the potential for improving IUD performance through the addition of pharmacologic agents are discussed. The mechanisms of action of IUDs, particularly of the copper and the progesterone-releasing devices, are reviewed. The development of improved intrauterine contraceptive devices will depend on an understanding of these mechanisms of action. In order to determine the optimal design of intrauterine contraceptives, the effects of the pharmacologic agents will also have to be evaluated, both separately and in combination with the carrier (vector).

INTRODUCTION

Modern intrauterine contraception dates back nearly 50 years to the development of silkworm-gut rings and tightly wound silver wire spirals by Gräfenberg (5), and rings of silkworm-gut and later of flexible metals and synthetic plastics by Ota (21). Although both Gräfenberg and Ota demonstrated that their intrauterine devices (IUDs) were highly effective, nearly 30 years passed before any major international efforts were directed towards the development, testing, and evaluation of intrauterine devices. In the early 1960s, a number of improved devices were tested and evaluated, including the Birnberg bow, the Marguilies spiral, and the Lippes Loop (30). From 1962 to 1974, 3 international conferences (8, 27, 31), plus innumerable symposiums, have been held on the subject of intrauterine contraception, and over 5000 scientific articles have been published on the subject.

With respect to contraceptive efficacy, IUDs made of biocompatible materials without any pharmacologic action (nonmedicated IUDs) developed during the 1960s offered no significant advantages over the devices developed by Grafenberg and Ota. IUD research efforts during the 1960s and early 1970s did, however, provide a better understanding of the mechanisms of action of IUDs and a rationale for their future development and evaluation. It was recognized that the relevant clinical IUD parameters—pregnancy, expulsion, and removal for bleeding and/or pain—were so interrelated that any IUD design which increased IUD performance with respect to any one of these parameters would most likely produce a decrease in IUD performance with respect to the other parameters. The relationship between the clinical effectiveness of nonmedicated IUDs and their physical properties (length, width, thickness, rigidity) has been evaluated (8). However, the application of this knowledge to the development of an IUD that would minimize the rates of all clinical parameters has met with variable success (32).

How an IUD will perform can be predicted on the basis of its physical properties, but these predictions are not always confirmed by clinical trials. Even when there is uniform reporting of data, the performance of a given IUD varies among reported series (2). While some of these differences may be due to different methods of evaluation, others are both clinically and statistically significant. These differences may be attributed to differences in the populations evaluated, insertion techniques, and the criteria for classifying IUD-related events.

Based on what is known today about IUDs, it is doubtful that a significant improvement in overall performance can be brought about simply by changing the design of a nonmedicated device. The addition of pharmacologic agents to a carrier system (vector) shows a potential for improving the performance of IUDs. The contraceptive effectiveness of such an intrauterine contraceptive system would be primarily a result of the effects of the pharmacologic agents rather than the presence of the vector, a biocompatible foreign body without any pharmacologic action.

This paper was presented at the IX World Congress of Fertility and Sterility, Miami Beach, Florida, USA, April 12-16, 1977.

INTRAUTERINE PHARMACOLOGIC AGENTS AND VECTORS

Any pharmacologic agent used for intrauterine contraception must have one or more of the following properties. It must (1) be effective in preventing pregnancy, (2) be antimetrorrhagic, (3) affect uterine motility in order to aid in the retention of the vector, and (4) be active in microdoses in order that a sufficient amount of the agent may be stored in the vector and be released over long periods of time.

The effects of a pharmacologic agent will depend on the type of vector (carrier system) used and the effect of the vector per se with respect to pregnancy, bleeding, and retention.

Vectors may be classified into 3 general types as follows.

1. **Macrovectors** are associated with low pregnancy rates. Pharmacologic agents are added to these vectors to improve one or more other aspects of their performance. For example, the Spring Coil IUD, with a surface area of 1756 mm^2, is highly effective in preventing pregnancy, but it is associated with high removal rates for bleeding (12). Antimetrorrhagic drugs could be added to the Spring Coil in order to reduce the incidence of removal for bleeding.

2. **Carrier vectors** are devices which are ineffective alone, but which become effective with the addition of a pharmacologic agent. For example, the "T" IUD is associated with a 1-year pregnancy rate of 18.2 per 100 women (32), but the addition of 200 mm^2 of copper wire reduces this rate to about 0.9 to 3.0 per 100 women (20).

3. **Microvectors** are devices which have no contraceptive value alone; contraception is provided almost entirely by the addition of a pharmacologic agent. The principal function of the vector is to release the agent at a steady rate within the uterine cavity. Such systems would include encapsulated pharmacologic agents (34).

Pharmacologic agents are classified according to their primary effects: contraceptive, antimetrorrhagic, or antiexpulsive.

Adding pharmacologic agents to intrauterine devices has modified the already established relationships between the physical properties of a device and its contraceptive effects and side effects. For example, the "7" and "T" vectors are associated with different pregnancy and expulsion rates, depending on the quantity of copper added to the vector and on the location of the copper on the device (20). Increasing the amount of copper modifies uterine motility and placement of the copper on the upper arms of the "T" or "7" devices affects expulsion rates (36). Although the accumulated evidence does not indicate that copper has antimetrorrhagic effects (28), a reduction in uterine motility may also result in less bleeding.

PHARMACOLOGIC AGENTS

To date only 2 pharmacologic agents, copper and progesterone, have been extensively evaluated for intrauterine contraception. These agents have been evaluated primarily using the "T" or "7" devices as vectors. The addition of copper or progesterone to the "T" vector significantly lowers the pregnancy rate. The 1-year pregnancy rate for the plain "T" is 18.2 per 100 women; for the Cu-T-200, it is 0.9-3.0 per 100 women; and for the Progestasert® (a "T" device which releases progesterone at a rate of about 65 mcg/24 hours), it is 1.9-2.5 per 100 women (33, 35).

Contraceptive agents

Both copper and copper combined with zinc are effective contraceptive agents when used with the "T" or "7" vectors. The use of copper has been extensively reported in the literature (20). The combination of copper (200 mm^2) and zinc (47 mm^2) added to the "7" vector is associated with a lower pregnancy rate than copper used alone (14). Studies are being conducted to evaluate the optimal placement of the 2 metals on the vector. It appears that a combination of copper and zinc creates a battery type effect in the uterus and affects the electropotential of the uterus and uterine motility (38). Although the copper-zinc combination is effective in preventing pregnancy, transitory metaplasia has been observed in some women who have used it. The primary change noted in women who have used the copper-zinc device is the large number of proliferative endometriums in the luteal phase of the menstrual cycle (14). Whether this indicates a specific effect of zinc on the endometrium or whether it indicates suppressed ovulation is not known at this time. Additional studies are being conducted to further evaluate the effects of zinc on the endometrium.

Based on the results of reported studies, progesterone appears to be the most adequate steroidal agent for contraceptive use. The Progestasert®, a "T" vector with a reservoir on the vertical stem which releases about 65 mcg of progesterone every 24 hours, is associated with a 1-year pregnancy rate of 1.9-2.5 per 100 women (23). The release rate of progesterone does not inhibit ovulation. Based on reported rates of expulsion and removals for bleeding, progesterone appears to be the most adequate steroidal agent for contraceptive use. The Progesta- the Progestasert® IUD are currently being evaluated and include devices which release lower amounts of progesterone over longer periods of time.

The synthetic progestogens, d-norgestrel, megestrol acetate, norethindrone, and methylnorgesterone in doses that do not inhibit ovulation, have bee evaluated for intrauterine contraception (3, 17). When released from silastic capsules carried on a "T" vector

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or used in silastic subcutaneous implants, these progestogens are associated with relatively high rates of ectopic pregnancy (Table I), and thus appear to be poor intrauterine contraceptive agents. A similar problem has been observed with the Progestasert® IUD (29).

Antimetrorrhagic agents

Nilsson and Rybo (18) demonstrated that metrorrhagia can be controlled by the oral administration of antifibrinolytic agents such as epsilon amniocaproic acid (EACA), trans-4-amino-methyl-cyclohexane carboxylic acid (AMCA) and paramino-methyl-benzoic acid. Ragab and Thomas (24) subsequently showed that the release of AMCA, at an average daily rate of about 4 mcg, from the Spring Coil IUD (a macrovector) significantly reduced the removal rate for bleeding from about 10 per 100 women to 1.1 per 100 women at 1 year. The importance of these studies is that they demonstrate the practicability of releasing small amounts of antifibrinolytic agents from a vector directly into the uterine cavity. If a release rate of about 4 mcg per day is sufficient to reduce the incidence of IUD-associated bleeding events, then it may be practicable to use carrier vectors such as the "T" or "7" to deliver drugs for 5 years or longer.

Further studies are being conducted to evaluate the intrauterine release of microgram amounts of EACA and AMCA. In these studies, the drug is released from a silastic sleeve on the Lippes Loop D (a macrovector). These studies will not only evaluate IUD associated events, e.g. removals for bleeding, but will also quantify blood loss throughout the menstrual cycle. To evaluate the effects of the antifibrinolytic agents (15), blood loss studies will also be conducted for a group of women who have a plain Lippes Loop D.

Recent unpublished reports (22) have indicated that, when released at an average daily rate of 65 mcg from a "T" carrier vector, progesterone does have some antimetrorrhagic properties.

Antiexpulsive agents

To date, IUD research has focused on physical modifications to IUDs to make them less traumatic and to improve their retentive properties. Pharmacologic agents to improve IUD retention have not been investigated, except for zinc which appears to have an effect on uterine motility when in contact with the uterocervical junction (14, 38).

ANTIFERTILITY MECHANISMS OF IUDs

The mechanisms of action of nonmedicated (biocompatible) intrauterine devices differ in the different species studied. These mechanisms have been discussed in the 3 international conferences on IUDs and in many research papers (8, 27, 31).

Until 2 years ago, it was accepted that in humans, as well as in rodents, an intrauterine foreign body produced an outpouring of acute and chronic inflammatory cells into the uterine fluid and that the product of their cytolysis was toxic to the blastocyst and prevented implantation (16). This no longer seems relevant in primates or human beings (4, 11), since in severely polymorph-depleted rats induced with rabbit antisera to rat neutrophils, the IUD works adequately (26). Thus it appears that the inflammatory process plays a minimal role, if any, in the mechanism of action of IUDs. Although there is no uniform agreement on the mechanisms of action of nonmedicated IUDs, the following may partially explain their contraceptive mechanism and metrorrhagic action:

1. An alteration in endogenous steroidal metabolism (11)
2. An accelerated production of uterine prostaglandins that would induce an anticipated menstrual period (26)
3. The fibrinolytic activity induced by IUDs (13)

Most of the experiments performed to investigate the mechanisms of action of copper and progesterone

Table I. Pregnancies with the "T" vector loaded with 4 different progestogens

Progestogen	No. of Patients	Woman-Months of Use	Pregnancies: Intrauterine No.	Intrauterine Rate*	Ectopic No.	Ectopic Rate*
Megestrol acetate	215	1 314	2	1.8	2	1.8
D-norgestrel	83	524	1	2.3	1	2.3
Norethindrone	176	893	4	5.4	1	1.3
Methylnorgesterone	44	252	1	4.8	0	0.0
Total	498	2 983	8	3.3	4	1.7

* *Pearl index.*

Source: Reference 3, Croxatto, H. and Diaz, S., 1976.

have attempted to dissociate the action of the vector from that of the pharmacologic agent. Hagenfeldt and Landgren (7) recently published a review of the local uterine changes induced by these substances. The modifications to the endometrium differ in the proliferative and secretory phases of the menstrual cycle and appear to be related to changes in concentration of the different cations, enzymes, and steroidal receptors of the mucosa.

Copper devices produce a marked increase in endometrial copper and a decrease in endometrial zinc in the secretory phase of the menstrual cycle (18). The enzymes, alkaline phosphatase and β-glucoronidase, decrease in the secretory phase, and the acid phosphatase activity increases in the proliferative phase (7). Glycogen content is increased, but there is an inhibition of the α-amylase activity (25). Effects on the steroidal receptors can be demonstrated, but seem to be specific for each species. Kinetic studies in the rabbit (19) have demonstrated that copper is a competitive inhibitor at the receptor level, affecting the progesterone more than the estrogen receptors, which could explain the morphologic suppression of the progestational effect in this species (37). Also, the greater stability of the estrogen receptor in the presence of copper would explain the increased estradiol uptake in the rat uteri with a copper-bearing IUD (1).

Progesterone-releasing devices produce a decrease in endometrial zinc, but the manganese levels are increased in the secretory phase. The alkaline phosphatase activity and β-glucoronidase activity are depressed in the proliferative and secretory phases, while acid phosphatase activity is increased in both phases (7).

The effects on the hormonal receptors indicate a reduction of estradiol in both phases and an increase in the progesterone concentration. This suggests an interference with the synthesis of endometrial receptors to endogenous estradiol (7). Morphologic evaluation shows a decidual transformation with atrophy of the glands.

Although the detected effects could explain some of the biologic effects observed, they do not answer the question of why endouterine copper or progesterone does not produce 100% inhibition of fertility.

Table II. Effects of copper (200 mm²) as an intrauterine contraceptive

Events	Number	%
Pregnancy	1	3.1
Expulsion	4	12.4
Removal	2	6.3
Bleeding	0	0.0
Other medical	1	3.1
Other personal	1	3.1
Woman-months of use	348	
Number of patients	32	

Source: Reference 34, Zipper, J. and Medel, M., 1976

EVALUATION OF PHARMACOLOGIC AGENTS

Although a number of different pharmacologic agents have been proposed and evaluated for intrauterine contraception, the effects of these agents per se have not been adequately evaluated. A rational approach to the evaluation of various pharmacologic agents would first include an independent assessment of the effects of the vector and the effects of the agent. If on the basis of these tests the pharmacologic agent has the potential for improving IUD performance, then tests to evaluate the combined effects of the carrier and the pharmacologic agent would be conducted. If the effects of the carrier and the agent cannot be independently assessed, future research aimed at improving the performance of intrauterine contraceptive devices will necessarily be conducted on a trial-and-error basis.

The addition of 200 mm² of copper to the "1" vector significantly reduced its pregnancy rate. However, in spite of the wide use of copper for intrauterine contraception, the effects of copper per se have not been evaluated. In recent years research efforts have been directed towards improving the efficacy of IUDs by modifying IUD designs and by adding varying amounts of copper to existing designs. In an attempt to evaluate the effects of copper, Zipper and Medel (34) evaluated the effects of plain copper as an intrauterine contraceptive. The "device" consisted of a 32 cm piece of 0.2 diameter copper wire wound around a 0.1 mm diameter polyethylene thread. The device was 2.5 cm long with a surface area of 200 mm². The device was anchored to the uterine fundus. Based on the results of 32 insertions of this device (see Table II), it appears that the contraceptive efficacy of the Cu-7-200 and Cu-T-200 IUDs is a result of the action of the copper and not the vector. The associated pregnancy rate of the device (Pearl index) was 3.1 (see Table II) per 100 woman-years, which is only slightly higher than the rates for the Cu-T-200 and Cu-7-200 IUDs. Additional trials similar to the above will be needed to determine the optimal amount of exposed copper (which is related to the amount of Cu^{++} released) needed to minimize pregnancy, expulsion and removal rates.

Similar experiments will have to be conducted to evaluate the effects of other agents.

COMMENT

In view of the known limitations of IUDs, the focus of future research will be on the development of intrauterine contraceptive systems in which the effects of the vector are enhanced through the addition of pharmacologic agents.

Today there are a number of IUDs in general use which are associated with acceptably low pregnancy rates. However, the problem common to all IUDs is abnormal bleeding events. Tolerance to IUD-related bleeding may vary among women in different cultures. Nevertheless, IUD removals for bleeding-related events is one of the leading reasons for IUD discontinuation. Therefore, the order of priorities for future research will be to design intrauterine contraceptive systems which minimize the incidence of bleeding, expulsion, and pregnancy. This is exactly the reverse of the order of priorities during the initial stages of IUD development during the 1960s.

For intrauterine contraceptive research to advance in a rational manner, the vectors' mechanisms of action must be more clearly understood. Given an understanding of these mechanisms, specific pharmacologic agents may be selected for evaluation and testing. These tests should evaluate the optimal dosage of the pharmacologic agent, the effects of these agents both at the uterine level and systemically, the potential toxicological effects of these agents, and the best type of vector to be used to deliver the pharmacologic agent.

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IUD Insertions by Midwives: Five Years' Experience in Santiago, Chile

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ABSTRACT

Pastene, L., Rivera, M., Zipper, J., Medel, M. and Thomas, M. (Hospital Sotero del Río, Puente Alto, Chile, and the International Fertility Research Program, Research Triangle Park, North Carolina, USA). *IUD insertions by midwives: five years' experience in Santiago, Chile.*
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This report includes data on insertions of Lippes Loop D, Copper-7, and Copper-T intrauterine devices (IUDs) performed by certified nurse-midwives and physicians with comparable levels of training and experience in inserting IUDs. Net 1-year pregnancy, expulsion, and removal rates were used to compare the experiences of the 2 groups. There were no significant differences between the groups in most of the event rates or in the overall method discontinuation rates. The authors conclude that, with adequate training and experience, nurse-midwives can provide this family planning service with no additional risk to patients.

INTRODUCTION

One of the major disadvantages of using intrauterine contraceptive devices (IUDs) in family planning programs is that in most countries they can be inserted only by physicians. In countries where medical resources are scarce, this requirement is a major limitation to providing IUDs within a family planning program. Many programs have trained and used nurses, midwives, and other paramedics to perform IUD insertions. To date, none of these programs have returned to a program in which only physicians are allowed to insert devices.

Since 1968, certified nurse-midwives have routinely performed IUD insertions in the Chilean National Health Service Maternity Hospital and satellite clinics in the Southern Region of Santiago. These personnel have inserted the 3 most commonly used IUDs: the Lippes Loop D, the Copper-7 (Cu-7), and the Copper-T (Cu-T). This report compares the experiences of nurse-midwives and physicians in inserting these devices at the same hospital. A total of 96 Loop D, 174 Cu-7, and 363 Cu-T devices were inserted by midwives. Correspondingly, physicians inserted 399 Loop D, 340 Cu-7, and 470 Cu-T devices.

MATERIALS AND METHODS

Subjects were not randomly assigned to either the nurse-midwife or physician groups. On days when a physician was in attendance at the hospital or clinic, he performed the IUD insertions; otherwise, insertions were performed by the nurse-midwives.

The nurse-midwives and physicians used the same criteria for selecting women for an IUD insertion. IUDs were usually inserted postmenstrually, and both midwives and physicians used a standard insertion technique.

For each device type, age and parity distributions of the women whose IUDs were inserted by nurse-midwives or physicians were similar, with the exception of the age distributions of the Loop D acceptors. The mean age of Loop D acceptors whose IUDs were inserted by nurse-midwives was 28 compared to 25 for those whose IUDs were inserted by physicians; the former group was also somewhat more parous, though not significantly so. For all IUD acceptors, the mean age was approximately 26 years and the mean parity was 2.6 live births. Age and parity distributions of each group are given in Table I.

Comparison of the 2 groups of inserters by device type was made using 1-year net event rates. Differences cited as statistically significant are significant at the 0.1 level.

RESULTS

For all 3 device types, continuation rates among women whose IUDs were inserted by nurse-midwives were approximately 83 per 100 women at the end of 1 year. The continuation rates among women whose

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IUDs were inserted by physicians ranged from 79 to 89 per 100 women at the end of 1 year. Approximately 10 per 100 women were lost to follow-up at the end of 1 year. Net event rates and other summary data pertinent to this study are shown in Table II.

Pregnancy

The 1-year pregnancy rates for the Loop D groups were significantly different, 9.3 per 100 women for the nurse-midwife group and 2.2 per 100 for the physician group. Ten (91%) of the 11 pregnancies were accounted for by 1 nurse-midwife who performed 79 insertions. Experiences with the copper devices were similar for the 2 acceptor groups.

Expulsion

Expulsion rates for the nurse-midwife group were significantly lower than the rates for the physician group for Loop D insertions, but significantly higher for Cu-7 insertions. For the Cu-T, the expulsion rate was higher among patients whose IUDs were inserted by the nurse-midwives but not significantly so. One-year expulsion rates for the nurse-midwife group ranged from 4.3 to 8.1 per 100 acceptors. For the

Table I. Age and parity distributions by insertion group and type of device

	Lippes Loop D		Copper-7		Copper-T	
	Nurse-Midwife (N=96)	Physician (N=399)	Nurse-Midwife (N=174)	Physician (N=340)	Nurse-Midwife (N=363)	Physician (N=470)
Age						
< 20	5	56	27	53	44	57
20-24	21	149	68	125	127	167
25-29	30	109	54	81	93	130
30-34	28	38	17	44	58	68
35-39	7	29	6	26	32	37
≥ 40	5	18	2	11	9	11
Mean	28.3	25.6	24.3	25.5	26.0	25.9
Parity						
0	1	4	0	1	5	9
1	10	108	43	65	86	126
2	23	139	59	101	116	154
3	17	74	33	66	79	97
4	10	28	18	40	26	37
≥ 5	35	46	21	67	51	47
Mean	3.8	2.6	2.6	3.0	2.7	2.5

Table II. Net cumulative continuation rates per 100 IUD acceptors by device type and insertion group

	Lippes Loop D		Copper-7		Copper-T	
	Nurse-Midwife (N=96)	Physician (N=399)	Nurse-Midwife (N=174)	Physician (N=340)	Nurse-Midwife (N=363)	Physician (N=470)
Pregnancy	9.3 (3.2)*	2.2 (0.8)	3.2 (1.4)	3.1 (1.0)	2.3 (0.8)	2.2 (0.7)
Expulsion	7.0 (2.8)	12.4 (1.7)	8.1 (2.2)	2.5 (0.9)	4.3 (1.1)	2.7 (0.8)
Removal						
Bleeding/Pain	1.1 (1.1)	2.2 (0.8)	1.2 (0.9)	2.5 (0.9)	2.3 (0.8)	3.8 (0.9)
Other medical	0.0	1.4	1.3	0.6	2.3	2.9
Planned pregnancy	0.0	0.8	3.3	1.6	3.5	2.7
Personal	0.0	1.9	0.0	0.6	2.0	0.4
Continuation	86.2 (4.1)	79.1 (2.1)	82.8 (3.0)	89.1 (1.7)	83.3 (2.0)	85.2 (1.7)
Cumulative woman-months of use	956	3888	1768	3669	3844	5043
Admission period	Jan. 1969-Oct. 1971		June 1970-Dec. 1970		Oct. 1969-Apr 1971	

* *Figures in parentheses are standard errors.*

physician group, the rates ranged from 2.5 to 12.4 per 100 acceptors.

Removals

No consistent pattern of differences was noted between the 2 inserter groups with respect to personal removals or for medical removals other than for bleeding or pain. Removals for bleeding and/or pain for the 2 inserter groups were not significantly different, but acceptors whose devices were inserted by physicians had higher rates of bleeding/pain removals than those whose devices were inserted by nurse-midwives.

DISCUSSION

Results of this analysis indicate that the nurse-midwife can participate safely and effectively in an IUD insertion program. However, the significantly higher Loop D pregnancy rates and Cu-7 expulsion rates among women who had IUDs inserted by nurse-midwives suggest that continued monitoring of nurse-midwife personnel in this type of program is needed to identify those who need additional training in inserting a particular device. Retraining was clearly indicated for the nurse-midwife who inserted 79 Loops with 10 (12%) resulting in a device failure leading to pregnancy. This monitoring, of course, should include physicians who may also need additional training. The high expulsion rate in the physician-inserted Loop D group was accounted for by 2 physicians: more than 20% of the devices they inserted were expelled.

Other studies (1-3, 5) have also suggested that nurse-midwives can effectively perform IUD insertions. However, Rosenfield (4) has indicated that successful programs depend primarily on good training and experience. A training period of from 4 to 6 weeks is recommended. Training should include not only proper insertion techniques, but also recognition of women who have contraindications to IUD use or who have conditions that may make inserting an IUD particularly difficult. A suggested checklist is shown in Fig. 1.

It should be recognized that since doctors are often involved in the most problematic cases, studies of this type, as well as those previously reported, are usually biased in favor of the nurse-midwife. Hence, doctors' event rates may tend to be higher than normal because their patients are at higher risk of expulsion or bleeding/pain removal than those with uncomplicated insertions. However, the appropriate use of nurse-midwives in family planning programs can appreciably increase the availability of family planning services and can, at the same time, increase the availability of other medical services by allowing the physician to make more efficient use of his time.

CHECKLIST FOR SCREENING IUD CANDIDATES

	No	Yes
Check the following by history:		
Increased menstrual or intermenstrual bleeding	☐	☐
Bleeding after intercourse	☐	☐
Last menstrual period (LMP) more than 4 weeks ago	☐	☐
Heavy vaginal discharge	☐	☐
Check the following by examination:		
Marked cervical erosion	☐	☐
Cervix bleeds on contact	☐	☐
Unusually large uterus	☐	☐
Adnexal or abdominal masses	☐	☐

Note: If answers to all questions are NO, insert the IUD. If the answer to any question is YES, refer the woman to a physician.

Fig. 1. Checklist for screening IUD candidates.

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EXPERIENCE WITH POSTPARTUM IUDS AT JOSE FABELLA MEMORIAL HOSPITAL, MANILA

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This work was supported in part by the International Fertility Research Program (AID/csd 2979).

INTRODUCTION

In the 1960's the Population Council implemented a postpartum IUD insertion Program that created widespread interest in this contraceptive method (4,5). Although interest has decreased over time, probably because of the high expulsion rate (25% of more) reported among patients with immediate postpartum insertions(5), the method offers many advantages. The high expulsion rate should not preclude further development of this method. On the contrary, it should be a challenge to investigators to create new designs which would correct this specific disadvantage (3).

The Jose Fabella Memorial Hospital in Manila and the International Fertility Research Program are presently making a concerted effort to find an IUD system that provides good retention in the immediate postpartum. The hospital is well suited for the study because of its heavy case load (it has an average of 100 deliveries a day) and the popularity of intrauterine contraception in Manila.

MATERIALS AND METHODS

In the study currently underway, all insertions are made immediately after delivery of the placenta. Four types of IUDs--the LEM, the postpartum "T", the Multiload, and the modified Lippes Loop D--are being studied, with the standard Lippes Loop D serving as a control.

One important objective of this study is to determine the safety and effectiveness of adding biodegradable extensions to standard IUDs as a means of preventing expulsion before the uterus has involuted to its normal size. Since

development and animal testing of the biodegradable material has not been completed, the Loop D was modified with silastic 382 instead of a biodegradable material.

All of the IUDs, except the LEM, are inserted by hand using a technique similar to the one reported by Burnhill (2). The Lem is inserted using an inserter tube.

RESULTS

Results from a study of 1359 LEM devices inserted postpartum from April 1973 to April 1974 were previously reported (1). Although the percentage of women expelling the LEM within 3 months was 8.6, the one-year gross expulsion rate per 100 users was 20.6. The six-month expulsion rate was 17.2. There was no evidence that either age or parity affected the performance of the LEM relative to expulsions. Although the LEM proved to have reasonable retention ability relative to experiences with other IUDs in the immediate postpartum, the pregnancy rate for the device in this clinical setting was 6.4 per 100 women at the end of one year. Most of the pregnancies occurred during the second six months of use. Perhaps, some design modification is in order.

Preliminary life table expulsion rates for the LEM and the modified Lippes Loop D are given in the following table. Since the start of the LEM series in 1973, the demographic characteristics of IUD acceptors have changed. The average age of women using the modified Lippes Loop D is 23 compared to 27 for LEM acceptors; the average parity of Lippes Loop acceptors is 2.4 down 20% from the average of 3.0 for LEM users.

DISCUSSION

Three-month expulsion rates for the modified Lippes Loop D inserted immediately postpartum are similar to those obtained with the LEM, but the pregnancy rate is expected to be considerably lower. Preliminary results from a study of women who had plain Loop D's inserted by hand indicate that the anterior-posterior projections to the device, not the insertion method, are responsible for the reduced expulsion rates. The plain Loop D has an expulsion rate of 11.0 per 100 women compared to 3.9 for the modified Loop D at 2 months.

When this series is completed the LEM, the postpartum "T", the Multiload, and the plain and modified Lippes Loop D with biodegradable extensions will be clinically tested under standardized conditions. The results will be computer analyzed. This information will provide a basis for prescribing postpartum IUDs and for making design adjustments necessary to further reduce expulsions and side effects. Thus, by testing a variety of IUDs designed for improved postpartum retention under closely controlled clinical and experimental conditions, we hope to find an IUD design that will reduce to an acceptable level the high expulsion rates that have acted as a deterrent to widespread acceptance of postpartum IUD insertion.

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NET EXPULSION RATES FOR
IMMEDIATE POSTPARTUM INSERTION

Months After Insertion	Rate Per 100 Women		
	LEM	Modified Loop	Lippes Loop D
1	1.5	1.9	5.0
2	7.8	3.9	11.0
3	10.1	9.1	

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POST "SPONTANEOUS" ABORTION USE OF THE INTRAUTERINE MEMBRANE CONTRACEPTIVE DEVICE

By

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Abstract

The safety and efficacy of the postabortion (inevitable or incomplete) insertion of the intrauterine membrane (IUM) device was evaluated in a study of 127 first insertions. Although the postabortion insertion of the IUM appeared to be a safe procedure, the device was associated with relatively high rates of pregnancy, expulsion, and removal/or pain and/or bleeding, and does not appear to be satisfactory for use after treatment of an incomplete abortion. The six-month life-table rates for these events were 4.3, 3.9, and 14.4 per 100 women, respectively.

I. INTRODUCTION

Each year, the University Hospital of the El Salvador School of Medicine treats over _____ women who are admitted with a diagnosis of inevitable or incomplete abortion. Most of these abortions are not spontaneous but are probably illegally induced. The consequences of an illegally induced abortion are well-known and include death and prolonged hospitalization for treatment of complications. Although all contraceptive methods may be safely initiated after an induced abortion (1), few investigators have evaluated the safety and efficacy of various contraceptive methods initiated immediately after treatment of a "spontaneous" abortion.

In 1973, a pilot program was started at the University Hospital to evaluate the immediate insertion of intrauterine devices (IUDs) after treatment of an inevitable or incomplete abortion. In a previous communication (2), the authors evaluated use of the Dalkon Shield and found it to be acceptable as a postabortion contraceptive. In 1975, a small trial of the intrauterine membrane (IUM) contraceptive device - an experimental IUD - was initiated. This report presents our initial evaluation of the IUM as a postabortion contraceptive.

II. METHODS AND MATERIALS

From October 1975 to October 1976, 127 first insertions of the IUM were performed for patients after treatment an/or inevitable or incomplete abortion. The IUM (Figure 1) is a heart-shaped membrane with six horizontal pleats, press-formed from Alathon-20 polyethylene sheets. The device has a

monofilament string attached to a V-shaped member which forms its lower edge. The IUM has a surface area of _____ mm^2, and its maximum longitudinal and lateral dimensions are _____ mm and _____ mm, respectively.

Definitions

All abortions, whether septic or aseptic, inevitable or incomplete, are designated as incomplete. Gestational age was estimated by the physicians who treated the incomplete abortions. Life-Table methods were used to evaluate the efficacy of the IUM. Only the six-month pregnancy, expulsion and removal rates were computed, since six-month follow-up data had been obtained for only 64 (50.4%) of the patients before the study was completed (April 1977).

Subjects

Most patients were multiparas, 20-29 years of age, treated for incomplete abortion during their first trimester of pregnancy (Table I). All but one subject reported at least one previous incomplete abortion.

Procedures

The incomplete abortions and IUM insertions were performed in a standard manner by the residents and house staff of the University Hospital. The incomplete abortions were treated by dilatation and curretage (D&C); 42.5 percent of these procedures were performed under general anesthesia. IUMs were not inserted at the time of D&C, but were inserted prior to the patient's discharge from the hospital, usually within 24 hours of the D&C. Prophylactic antibiotics were not routinely administered either before or after the D&C and/or IUM insertion. Before the D&C, prophylactic antibiotics were administered to 26.7 percent of the patients. This included three patients with a diagnosis of

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septic abortion. There were no serious complications such as uterine perforation or sepsis attributable to either the D&C or the IUM insertion procedures. All patients were requested to return for routine follow-up visits at 1, 3, 6, and 12 months after the IUM insertion.

III. RESULTS

Among women who returned to the University Hospital for at least one follow-up visit (93.3%) there have been 8 pregnancies, 4 expulsions, and 44 removals of the IUM, including 19 removals for bleeding and/or pain (Table II). Acute pelvic infection occurred for one patient, whose IUM had been removed after one month, when she complained of pain. Pelvic infection was also the diagnosis for four women examined at the time of routine follow-up visits at one, two, five, and nine months after the IUM insertion. None of these IUMs were removed, but the patients were treated with antibiotics, and their recovery was uneventful. Another woman, whose IUM was removed after one month because of prolonged bleeding, had also developed severe dysplasia.

Difficulties in inserting the IUM were infrequent. For one patient, difficulty in introducing the inserter in the cervix was encountered. For three others the IUM had to be removed and reinserted. For two of the latter, it was observed that the string of the IUM was not visible at the external cervical os, and for the third, that the IUM had not been deployed into the upper uterine segment.

The six-month life-table rates for pregnancy, expulsion and removal are shown in Table III.

COMMENT

Based on the results of the present study, the insertion of the IUM following treatment of an incomplete abortion appears to be a safe procedure. Other than the one case where the patient developed an acute pelvic infection within one month of the IUM insertion, there were no potentially serious complications.

The IUM does not appear to be a satisfactory device for use after treatment of an incomplete abortion. The six-month life-table pregnancy, expulsion, and bleeding and/or pain removal rates were 4.3, 3.9, and 14.4 per 100 women, respectively. There rates are higher than the corresponding rates based on 259 first insertions of the Dalkon Shield, which we previously reported (2), when inserted in a similar group of women after treatment of an incomplete abortion. The pregnancy, expulsion, and removal for bleeding and/or pain rates for the Dalkon Shield were 3.5, 3.7, and 4.2 per 100 women. A comparison of the six-month rates for the IUM and Dalkon Shield indicates the removal rate for the IUM to be significantly ($p<.05$) higher. The use of other IUDs, such as the Multiload Cu-250, Cu-7-200, and Cu-T-200, which are commercially available, need to be evaluated for use in patients after treatment of an incomplete abortion. The apparent antimetrorrhagic properties of the copper may make these devices more appropriate for use in women who have been treated for an incomplete abortion than bioinactive devices such as the IUM and Dalkon Shield.

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SELECTED PATIENT CHARACTERISTICS

AGE (years)	NO.	PERCENT
< 20	34	25.8
20-29	77	58.3
30-39	19	14.9
Mean		
PARITY		
0	29	22.8
1-2	70	55.1
3-4	24	18.9
5+	4	3.2
Mean		
GESTATIONAL AGE (completed weeks)		
≤ 8	77	60.6
9-12	38	29.9
13.-16	8	6.3
17 and over	1	0.8
Unknown	3	2.4

TABLE II

NUMBER AND TYPE OF EVENTS

EVENT	NO.	PERCENT
Pregnancy	8	14.3
Expulsion	4	7.1
Removal		
Bleeding and/or Pain	19	33.9
Planned Pregnancy	9	16.1
Other Personal Reasons	16	28.6
TOTAL		100.0

TABLE III

NET CUMULATIVE 6-MONTH EVENT RATES

EVENTS	RATE PER 100 WOMEN		STANDARD ERROR OF RATE
Pregnancy	4.3		2.1
Expulsion	3.9		1.9
Removal			
Bleeding and/or Pain	14.4		3.5
Planned Pregnancy	1.1		1.1
Other Personal Reasons	12.1		3.3
Cumulative Women Months of Use		721.5	
Number of First Insertions		127	

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The use-effectiveness of copper IUDs

Introduction

Although intrauterine devices (IUDs) have been associated with serious and sometimes fatal complications, they are nevertheless a safe and effective method of contraception. Over the past years, changes in IUD design and improved insertion techniques and standards of medical care have reduced the incidence of serious IUD-related complications, such as cervical and uterine perforation and complications related to pregnancy with an IUD *in situ*.

Because serious IUD-related complications occur relatively infrequently, the most important events in evaluating different IUDs for use in family planning programmes are contraceptive failure, expulsion, and removal for medical reasons.

Since 1958, doctors and nurse-midwives at the Hospital Barros-Luco in Santiago, Chile, have inserted over 30,000 IUDs. These include, among others, the Lippes Loop D, Cu-T-200, Cu-7-200, and a number of variants of the copper IUDs containing different amounts of copper with or without the addition of zinc. The long-term use-effectiveness of three of these devices, the Lippes Loop D, Cu-T-200, and Cu-7-200, is examined in this report. These three were selected for evaluation because they are the most widely used IUDs in public and private family planning programmes. Also, sufficient experience has been accumulated with these devices to present five-year rates.

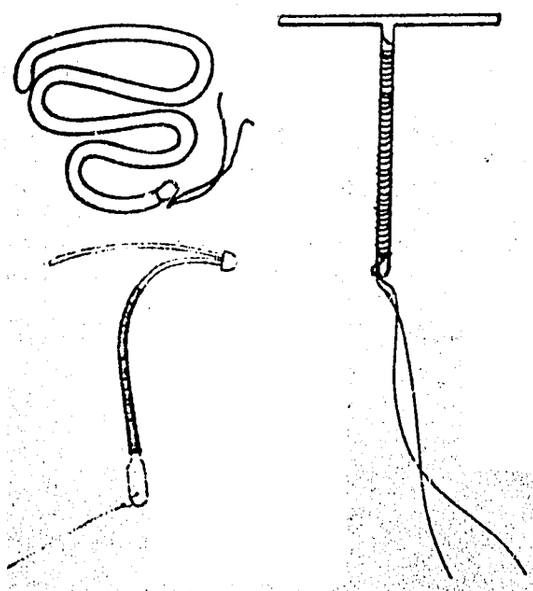

Fig. 1. Lippes Loop D, Cu-T-200, and Cu-7-200 IUDs.

Materials and methods

Pregnancy and discontinuation rates for all medical reasons are compared for 481 insertions (January 1969–November 1971) of the Lippes Loop D, 821 insertions (October 1969–October 1973) of the Cu-T-200, and 504 insertions (June 1970–August 1974) of the Cu-7-200. Both copper IUDs contain 200 mm² of filamental copper wound round the stem of the IUD (Fig. 1). All women had completed their last pregnancy at least eight weeks before the insertion.

Women who had a Lippes Loop D, Cu-T-200, or Cu-7-200 IUD fitted had a similar distribution of age and parity. The mean age of all women was 25·7 years, and parity 2·7 live births. Less than 1·0% of the women were nulliparas.

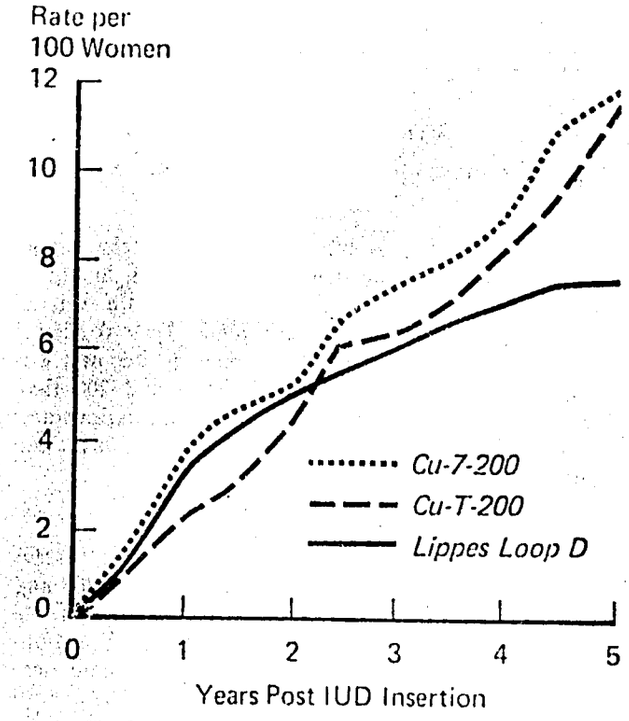

Fig. 2. Gross cumulative (life-table) pregnancy rates.

Pregnancy and discontinuation rates for all medical reasons were calculated using the life-table method. Rates for the three IUDs were compared using a procedure described by Azen *et al.*[1] The mean annual loss to follow-up rates varied from 3·2 per 100 women for the Lippes Loop D, to 11·1 for the Cu-7-200 users.

Results

The cumulative five-year pregnancy rates for the Lippes Loop D, Cu-T-200, and Cu-7-200 are shown in Fig. 2. The overall cumulative pregnancy rates were not significantly different ($p > 0·10$) for the three IUDs. The pregnancy rates and their standard errors at one, three, and five years are given in Table I. Cumulative pregnancy rates for the Cu-T-200 and Cu-7-200 did not increase more rapidly with increasing duration of IUD use.

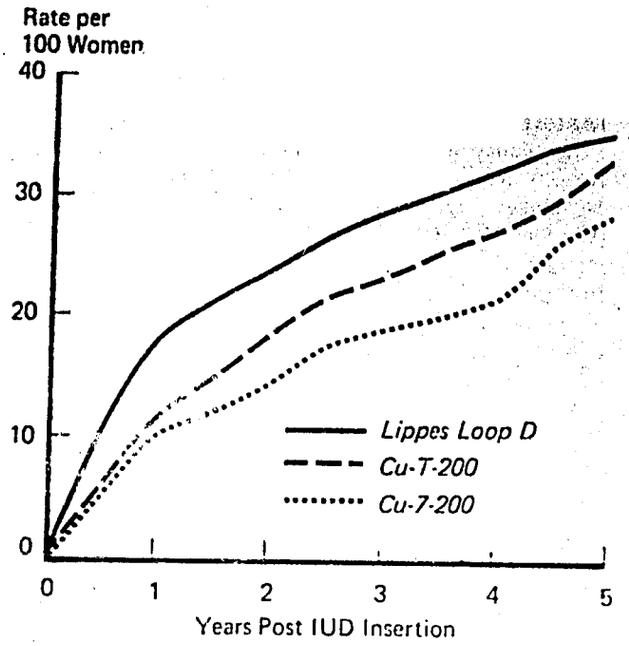

Fig. 3. Gross cumulative (life-table) medical discontinuation rates

The cumulative discontinuation rates for the Lippes Loop D, Cu-T-200, and Cu-7-200 are shown in Fig. 3. The overall cumulative discontinuation rate for all medical reasons was significantly higher ($p < 0 \cdot 10$) for the Lippes Loop D than either copper device, and was significantly higher ($p < 0 \cdot 10$) for the Cu-T-200 than for the Cu-7-200. The cumulative discontinuation rates for all medical reasons at one, three, and five years and their standard errors are given in Table I.

TABLE I. GROSS CUMULATIVE (LIFE-TABLE) PREGNANCY AND MEDICAL DISCONTINUATION RATES

Years after IUD insertion	Pregnancy rate			Medical discontinuation rate		
	Lippes Loop D	Cu-T-200	Cu-7-200	Lippes Loop D	Cu-T-200	Cu-7-200
1	3·8(1·0)	2·5(0·6)	3·4(0·9)	17·7(1·8)	11·6(1·2)	10·6(1·4)
3	6·1(1·3)	6·3(1·0)	7·5(1·4)	28·3(2·2)	22·8(1·6)	18·4(1·9)
5	7·5(1·5)	11·5(1·7)	11·8(2·1)	34·8(2·5)	32·5(2·1)	28·0(2·9)

Standard errors of rates are given in parentheses

Comment

Although it was initially recommended that IUDs containing filamental copper, such as the Cu-T-200 and Cu-7-200, be removed after two years because of the expected copper depletion, this study suggests that both these copper-containing devices provide adequate protection from pregnancy for up to five years. The overall five-year pregnancy rates were similar for the Lippes Loop D, Cu-T-200, and Cu-7-200. On the basis of pregnancy rates alone, all three IUDs are acceptable for use in a family planning clinic. However, because the cumulative discontinuation rate for all medical reasons was significantly lower for the Cu-7-200 compared to the other two IUDs, use of this device is perhaps preferable. It provided contraceptive protection for a greater proportion of the subjects over an extended period. One advantage of the Cu-T-200 and Cu-7-200 IUDs is that they are suitable for use in nulliparas and multiparas, whereas the Lippes Loop D is recommended only for multiparas. The apparent ease in inserting the Cu-T-200 IUD further recommends its use.

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ASSESSMENT OF INTRAUTERINE DEVICE CONTRACEPTION

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I. INTRODUCTION

The term "intrauterine device" (IUD) is recommended by the World Health Organization to describe a foreign body placed into the uterine cavity for contraceptive purposes and has replaced the older term "intrauterine contraceptive device" (IUCD) (1). One may look upon the IUD as the discovery of modern times, but in fact, folk and old medical literature is full of references to a wide variety of materials and agents that have been placed in the uterus for the purported management of gynecologic disorders as well as contraception. The literature on the safety and efficiency of intrauterine devices and reports on their merits or ill effects became voluminous. A number of devices were patented and each new one was claimed to be more efficacious, safer, and easier to insert than others.

In 1909, Richter in Germany described a device made from two or three strands of silkworm gut (2). This was probably the first IUD in the true sense of the word, but it was not used extensively and was soon forgotten. Another German physician, Pust, in 1923 described an intrauterine ring with a cervical extension, but again, this device was little used (3). The rebirth of the intrauterine device has been associated with yet another German physician, Gräfenberg, who published in 1929 a report on the use of his device in more than 2000 patients (4). A modification of the Gräfenberg device, the Ota ring, was introduced in Japan in 1934 (5). In both countries, these devices were the subject of great controversy.

Interest in intrauterine devices as a contraceptive lay dormant following this burst of interest in the late 1920s and early 1930s. Contraceptive practices were not encouraged and in most countries were overtly opposed. In 1959, Oppenheimer of Israel published the results of 28 years of experience with continuous use of his modification of the Gräfenberg ring (6). Almost simultaneously, another favorable report on IUDs was published by Ishihama in Japan (7). During the past 10 years, a number of programs have been undertaken to develop new devices of various shapes and sizes and to study their effectiveness and acceptability. Despite these variations in shape and in order to provide an acceptable degree of effectiveness, some IUDs made of relatively inert materials have had to be so large as to cause distortion of the uterine cavity resulting in undesirable and unacceptable side effects such as pain and bleeding. Findings show that a direct relationship exists between the surface area of the device and removal for reasons of pain and bleeding and pregnancy (8), as Figure 1 illustrates.

Because of the limitations associated with inert intrauterine devices, a new approach became necessary. Primarily stimulated by Zipper, a broader concept of intrauterine contraception has evolved (9). Zipper found that very small amounts of metallic copper placed within the uterus markedly inhibited fertility in women. Zipper's discovery has eliminated the dependence upon large inert devices. In contrast, it uses an intrauterine carrier for the active agent, the carrier contributing little, if any, to the total antifertility effect.

Today's practicing physician expects an intrauterine device to be easy to insert, to have good retention properties, to be effective in terms of low pregnancy rate, to have minimal side effects relating to bleeding and pain, and to be easy to remove if necessary.

Due to the time constraints of this paper, a complete review of all aspects of the IUD as a contraceptive is not possible. Therefore, the paper will be limited to the following topics: selection of a method, advantages of an IUD over other methods, timing of insertions, who should insert the device, type of IUD, and management of side effects.

II. SELECTING A CONTRACEPTIVE METHOD

In an industrial country with at least one doctor for every 600 inhabitants, where illiteracy is minimal, the great majority of the population have completed at least nine years of school, and per capita income is more than $1,500 a year, the selection of a contraceptive method is usually the result of a medical consultation. The woman living in a developed country who decides to regulate her fertility will find no dearth of doctors to consult. Her doctor, in turn, will have the time to explain to her how each method is used, its mechanism of action, and its possible side effects. The woman or the couple can then personally select the most suitable method. If the first selection turns out to be unsuitable, the woman has a good opportunity to consult her doctor again. Her doctor can then consider not only the method's effectiveness but also its acceptability to the patient. Since the man and woman are already knowledgeable, no time will be lost in motivating them; the second consultation itself is sufficient proof that they are motivated. If abortion has been legalized, as it has in many countries, the doctor knows that the failure of a recommended method will not necessarily result in an unwanted child. In this case, the doctor will be even less concerned with recommending the most effective method and more concerned about suggesting one that the patient will accept.

Even in a developed country a certain proportion of people, however small, cannot afford to pay for medical services. For these people, a government usually provides public health facilities that offer services of high quality and low cost. In such countries, led by a simple sense of human justice, public health personnel try to duplicate the attitudes that the private sector has for private patients. The woman who uses public health facilities like the private patient is given full freedom to choose among the various contraceptive methods known today. This has given rise to the so-called "cafeteria system", named after those American restaurants in which the customer chooses what he wants to eat from a variety of dishes displayed for his inspection. Could such a system be used in developing nations? Would it function in a just and proper way?

In Developing Nations

Selecting a contraceptive method for a mass program in a developing country will inevitably be a quite different process. Those responsible for the program will have to take cost into account, as well as method effectiveness and patient acceptability. Countries in the developing world rarely have more than one doctor for every 1,500 people. It is not unusual to find data that shows one doctor for each 5,000 or 10,000 inhabitants. The doctor is obliged to delegate a large part of his work to paramedical personnel, and his role as educator vis-a-vis the patient must be viewed as extremely limited.

The population that need contraceptive services have had little or no education and are thus totally ignorant of existing effective methods. Their attendance at clinics providing contraceptive services will depend, in large part, on educational campaigns promoted through mass media. If, because of an educational campaign or on the advice of friends or neighbors, these people

arrive at a clinic, they will most likely learn about a method without learning about its mechanism of action. In such clinics, because of limited time and personnel, groups are told only how to use a method and not how a method functions. The latter would probably not be understood, anyway, because the explanation usually involves complicated diagrams that make sense only to those who know basic anatomy.

The use of spermicides--whether jellies, suppositories, or foams--will become too expensive for this population over the long run. The diaphragm, with spermatocidal jelly added, is initially expensive and the spermatocide represents a continuing cost. Also, the use of the diaphragm requires a certain amount of privacy and this factor must be taken into account when patient acceptance is considered. It would be impractical and unrealistic to recommend a diaphragm to people who live in crowded conditions, often four or five to a room containing only one bed. Also, the care and cleaning of the diaphragm requires a clean water supply, which is not usually available in such conditions. However useful spermicides and diaphragms might be elsewhere, they should not be provided in mass programs in which cost is an important factor.

In Countries Where Abortion Has Not Been Legalized

In areas where abortion has not been legalized, failure of a method generally means either a clandestine abortion or the birth of a unwanted child. Since either outcome is undesirable, massive clinical programs should direct themselves to reversible methods with the highest effectiveness and to surgical sterilization. Among reversible methods, two are now in greatest demand: hormonal methods, whether via a daily pill or an injection, and intrauterine devices (IUDs). Past experience has shown that IUDs have the highest continuation-of-use rates (10); they require supervision that is continually less demanding

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and are less costly than hormonal products. For these reasons, IUDs are preferable for most mass programs.

For Nulliparous Women 18 and Under

When the moment to select a method arrives, it is essential to take into account the age of the woman who is asking for contraceptive protection. This point is sufficiently important to consider it in more detail (11).

Women with active sex lives, who are younger than 18 years but not yet mothers, generally react poorly to contraceptive pills, especially when the menstrual pattern is not yet well established or minor signs of androgenic syndrome are present. Injections of long-lasting hormones are not advisable, since the substance cannot be removed if symptoms indicate the woman should abandon the method. At ages in which the endocrine system is acquiring its mature equilibrium, any hormonal therapy should be used with the greatest caution. Intrauterine devices of small size, especially designed for women who have not had children, would probably be indicated for these women. It must be recognized, however, that the IUD very frequently causes pain and an increase in menstrual flow. Until we can control these side effects, the safest method appears to be the use of the condom by the husband or companion.

For Nulliparous Women 18 to 35

For women between 18 and 35 who have not had children, the pill seems to cause fewer problems than the IUD. But if the woman has had a pregnancy, an IUD should be recommended.

For Women of Proven Fertility at Any Age

If the desired family size has been reached, and the couple has made a firm decision not to risk a new pregnancy, sterilizaton of one partner might prove the best method (12). For mass programs, we believe that at any age, women of proven fertility should be encouraged to use the IUD as the best method for spacing pregnancies. The use of pills or long-lasting injections should be reserved for women who continue to expel the IUD (although this is rare after age 25, especially among women who have had children) or for women who have side effects requiring IUD removal or have specific objections to the IUD itself.

III. USE OF THE IUD

Thus, both cost and effectiveness appear to recommend IUDs, especially second generation devices, as a good method for mass programs (13). In addition, safety is also a feature of the device. If we analyze the mortality associated with an IUD with that of other contraceptive methods, the IUD has a very low rate, as shown in Table 1 (14). Besides these factors, the IUD is a reversible method, separates sexuality from unwanted conception, does not require repeated application or motivation, has no apparent long-term effect on return of fertility, and does not affect lactation. As Norman Haire so picturesquely pointed out more than 40 years ago, the IUD "is free from the anesthetic disadvantages of all other methods of contraception and does not interfere at all with the spontaneity of intercourse. It requires no preparation just before intercourse, which may take place equally well in the marital bed or on the sea-shore" (15).

Inserting the IUD

Inserting an IUD is a very simple procedure for experienced family planning personnel which is usually free from complications. Uterine cramps, pain, or

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pelvic discomfort may accompany insertion, especially if performed in haste. Usually these complaints last only a very short time. When a patient has severe discomfort, pain, or cramps, it may be necessary to remove the IUD to stop the local pain, uterine spasm, and mental anguish accompanying the sudden hypotensive episode. (It is useful to have available a bottle of "spirits of ammonia" to assist the recovery of the patient who experiences a hypotensive episode. Also useful are Coramine drops and/or Micoren drops or "pearls".)

It is believed that most uterine perforations occur at the time of insertion, or may be initiated at insertion. This is especially true in the case of women who have had one or more cesarean deliveries and in whom dehiscense of the uterine wall and/or intrauterine adhesions (synechiae) may facilitate the occurrence of perforation. Passive migration of the device through the uterine wall (myometrium) following partial perforation at the time of insertion can also occur and may be assisted by uterine contractions. These contractions, which are increased by the irritation produced by the foreign body, are reported with all devices. The frequency of perforation, however, varies according to device, clinic, and individual physician. The reported rates of IUD perforation range from 0.2 per thousand with the Cu-T to 8.7 per thousand with the Lippes Loop (16). While the type of device and the mode of insertion are no doubt directly related to the frequency of perforation, the most common causes of perforation are incompetence, carelessness, and ungentle or hasty handling by the person performing the insertion (17).

These causes lead to a consideration of who can best perform the insertion. A major problem in the developing countries has been the critical shortage of physicians available to provide health services. Because of this shortage, the

issue has been raised as to whether the physician must be the only person to perform such tasks as IUD insertion.

Accepted medical practice dictates that a careful medical history and a physical examination should be conducted before inserting an intrauterine device. However, there is no reason why a paramedic or auxiliary personnel such as midwives and obstetrical nurses cannot be trained to do this. Experience in Indonesia, Pakistan, Chile, Korea, and the United States shows that IUDs can be inserted by nurses and others without a significant increase in complications. Therefore, for performing a routine insertion, a well trained nurse or midwife is an acceptable alternative to a physician. However, a physician should be available to handle any problems or complications which may occur. Nurses or midwives trained to insert IUDs are of great importance in developing countries. While the doctor may be able to donate only part of his time to contraceptive services, the trained nurse or midwife can be used full-time and thus greatly increase the effectiveness of mass programs (18).

Timing of Insertions

It is often advised that IUD insertions be performed during the menstrual period. This has been suggested because the cervical canal is more open at this time during the cycle and because any bleeding that might be produced by the insertion would be masked by the menses. This interval has also been considered favorable since the possibility of a woman being pregnant during menstruation is unlikely (19).

It is inadvisable, however, to delay the insertion until the time of the next menstrual period by asking the prospective candidate to return during her

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menses, since this might force the woman to go without contraception or to use a less reliable method for part of a cycle, thus increasing the risk of pregnancy. Such a delay might also cause women to lose interest in contraception, the clinic, and its program, and fail to return at the time of menses. Depending on the local situation, postmenstrual and intermenstrual intervals are also frequently used for insertion in order to accomodate a large number of patients.

Postpartum and Abortion Insertions

Postpartum and postabortion insertions have been resisted in the past by physicians, who feared greater risk of uterine perforation, increased sepsis, and higher expulsion rates. Recent studies, however, have shown encouraging results, as shown in Figures 2 through 5 (20). Postpartum insertions may be "early", between 48 and 72 hours after delivery but before discharge from the hospital, or "immediate", performed directly after delivery of the placenta while the patient is still on the delivery table. The postpartum time is ideal for insertion because the woman is highly motivated toward contraception. Also, in most parts of the world, less than 10 percent of the women return for their routine postpartum visit, so if they are to accept a contraceptive method, it should be offered before hospital discharge.

The International Postpartum Program (IPP) has collected much information on postpartum insertions worldwide. Their information, based on more than 25,000 cases, shows that for pain, bleeding, and infection, no great difference exists between early insertions and delayed or interval insertions. Some reports have shown that uterine perforation does not appear to be more prevalent in early insertions, but expulsion rates are higher (21). Careful training of physicians in postpartum insertion and devices which have been modified to produce better postpartum retention should reduce expulsion rates.

Postabortion insertions may also be performed "early" or "immediate" (22). Many women are admitted to hospitals for incomplete spontaneous abortions and abortions induced outside of the hospital. These conditions caused physicians to refrain from postabortion IUD insertions because they expected an increased risk of infections. Studies have disproved this, however, and postabortion expulsion rates and complication rates are similar to those of delayed insertions.

The insertion technique itself is one of the most important factors in the effectiveness of postpartum and postabortion insertions (23). The IUD must be placed high in the fundus and not in the lower uterine segment. A longer inserter for postpartum use may help, especially for physicians or others with little experience. Studies are currently being conducted to determine if hand placement of an IUD reduces expulsion (24).

Potential Problems with an IUD

Regardless of the time of insertion, the patient should be informed of potential problems which may occur and what can be done about them. Unintended pregnancy may occur in one to three percent of patients with the device in utero. Pregnancy may also occur after unnoticed expulsion of the device. Expulsion occurs most commonly during menses, and, for this reason, the patient should be advised to examine herself periodically. She should always check for the thread of the IUD before resuming sexual relations after menses. From the many reported clinical studies of the IUD, it has become apparent that accidental or unwanted pregnancies occur more frequently (i.e., pregnancy or failure rate is higher) with smaller inert devices than with larger ones. The pregnancy rate is higher for younger women, and among women of the same age, it is higher for those who have higher parity.

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A question immediately arises concerning what should be done about these unwanted pregnancies. In view of the proven complications associated with pregnancies with a device in situ, removal of the device and early termination of the pregnancy is medically indicated. Any IUD wearer who becomes pregnant should be informed of the potential complications (25).

Bleeding and pain are the most common causes for terminating IUD use. When reported separately, removals for prolonged irregular bleeding are more frequent than removals for pain.

Menses tend to appear sooner and last longer than normal in women wearing IUDs, and the flow tends to be heavier after insertion. Intermenstrual bleeding and spotting may also occur. Generally speaking, if the experience of any woman with an IUD is long enough, she will, at one time or another, have an episode of spotting and/or bleeding. Most women can cope well with prolonged and more copious menses, especially if forewarned. However, some will request removal if there is even minimal disturbance of their usual menstrual pattern. Although many auxiliary therapies have been tried (e.g., temporary use of oral contraceptives, oral estrogens, Vitamin C, Vitamin K, riboflavin, iron, "psychological support", etc.), no serious evaluation has been made of the effect that any one of these measures might have in correcting the problem. If a woman requires auxiliary therapy or complicated staff efforts to assure continuation of IUD use, it may well be that an IUD is not suitable for that particular woman. If the device is removed, it is most important that the woman be immediately provided with another form of contraception (19).

Occasional cramping and pain beyond the time of insertion may be reported. In the great majority of cases, the pain is well tolerated and tends to disappear spontaneously after a few days. Cramps are more intense and frequent in nulliparous women than in parous women. To assist the patient with pain or cramps, it is advisable for the physician to recommend that the woman take aspirin. A dosage of up to two tablets every four hours is suggested and the aspirin is best taken with a mild antacid such as milk. If a mild antacid is not available, plain drinking water will do.

The occurrence of an inflammatory response or infection in the uterus and adnexa is another complication which may accompany IUD use. After bleeding and pain, pelvic inflammatory disease (PID) is the most frequently reported medical reason for removal of the IUD (26). The frequency of removal for this cause is virtually the same for all devices. Antiseptic measures and careful procedures during insertion will prevent the occurrence of infectious complications. However, in spite of care taken during IUD insertion, the endometrial lumen can become contaminated at this time (27). Since most women manifesting the disease after insertion have a record of a previous pelvic inflammatory episode, it is usually assumed that most post-IUD insertion episodes of pelvic inflammatory disease are recurrences of the previous condition. Pelvic inflammatory disease occurs more frequently among IUD users from the lower socioeconomic strata (28).

In most cases, properly selected antibiotic therapy administered with the IUD in place corrects the inflammatory process. While some physicians remove the device immediately before giving antibiotic therapy, such a course of action should be weighed carefully, since the manipulation required to remove the device may contribute to the spread of the disease and aggravate the infectious process.

During the decade of the 1960s, various IUD designs were developed, essentially by empiricism. Nonetheless, this search for an "ideal design" was stimulated by well defined performance requirements. A practicing physician expects an intrauterine device to be easy to insert, to have good retention properties, to be effective in terms of a low pregnancy rate, to have minimal side effects relating to bleeding and pain, and to be easy to remove if necessary. In order to fulfill these requirements, an IUD should have the following characteristics (29, 30):

1. Flexibility, so that it may be folded or temporarily reshaped to allow easy passage through the cervical canal without overly distorting it.

2. Sufficient "memory" characteristics in the material from which it is made to permit rapid return to the preformed shape following insertion.

3. A design and material composition that the contracting uterus cannot deform into a shape for easy expulsion and one that will not exert excessive force on the uterine cavity.

4. Sufficient rigidity or stiffness of material to prevent easy deformation by uterine contraction and, consequently, expulsion.

5. A size and surface area that will not disturb the uterus to a degree that causes cramping or bleeding.

Finally, because it is recognized that even with the greatest care there may be an occasional uterine perforation, devices must be of an open shape. A

closed ring or loop which perforates the uterus and is in the peritoneal cavity can lead to bowel capture, obstruction, and strangulation (31).

While many of the devices in use today are suitable for interval or post-abortion insertions, a postpartum device with higher retention rates is needed. Work is currently being conducted to develop and study standard devices modified with biodegradeable and permanent extensions to safely improve retention. Soft, flexible, biodegradeable extentions are being added to the Lippes Loop, the Copper-T, and the Copper-7 (24). Studies are being conducted to determine if the retention rate is significantly improved by the extensions. While work on the IUD is ongoing, the IUD is still an excellent option for mass family planning programs. Multiple types of IUDs should be made available, since no single type of IUD is suitable for all patients. Selection should be made considering each patient's age, parity, anatomical conditions, and puerperal status.

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TITLES AND L

Table I:	**Title:**	Title on table.
	Legend:	From: Tietze, C, Bongaarts, J & Shearer, B: Mortality Associated with the Control of Fertility. Fam Plann Perspect 8(1):6, 1976.
Figure 1:	**Title:**	Two-Year Pregnancy and Bleeding/Pain Removal Rates of Some Barium Polyethylene IUDs as a Function of their Surface Area. (Data from Cooperative Statistical Program of the Population Council and the International Fertility Research Program.
Figure 2:	**Title:**	Length of hospitalization in patients with abortions initiated out of the hospital.
	Legend:	From: Tatum, H J: Intrauterine Contraception. Am J Obstet Gynecol 112(7):1000, 1972.
Figure 3:	**Title:**	Highest temperature during hospitalization (with antibiotics). Abortions initiated out of the hospital.
	Legend:	From: Tatum, H J: Intrauterine Contraception. Am J Obstet Gynecol 112(7):1000, 1972.
Figure 4:	**Title:**	Distribution of fever for all patients in both groups. Abortions initiated out of the hospital.
	Legend:	From: Tatum, H J: Intrauterine Contraception. Am J Obstet Gynecol 112(7):1000, 1972.
Figure 5:	**Title:**	Ranges of temperature for all patients in both groups. Abortions initiated out of the hospital.
	Legend:	From: Tatum, H J: Intrauterine Contraception. Am J Obstet Gynecol 112(7):1000, 1972.

Table I

Mortality associated with pregnancy and childbirth, induced abortion, use of oral contraceptives and IUDs, and tubal sterilization, by age of woman

Age group	Pregnancy and childbirth*	Induced abortion†	Oral contraception‡	IUDs‡	Tubal sterilizations§
15-19	10.8	2.3	1.3	1.0	na
20-24	8.5	1.9	1.3	1.0	na
25-29	12.1	1.9	1.3	1.0	10.0-20.0
30-34	25.1	4.2	4.8	1.0	10.0-20.0
35-39	41.0	9.2	6.9	1.0	12.5-25.0
40-44	69.1**	10.1	24.5	1.0	15.0-30.0

* Ratio per 100,000 live births.

† Ratio per 100,000 first-trimester abortions.

‡ Rate per 100,000 users per year.

§ Ratio per 100,000 operations at beginning of age interval.

** The mortality ratio for all women aged 40 years or more was 78.5 per 100,000 live births.

Note: na = not applicable.

From: Tietze, C, Bongaarts, J & Schearer, B: Mortality associated with the control of fertility. Fam Plann Perspect 8(1):6, 1976.

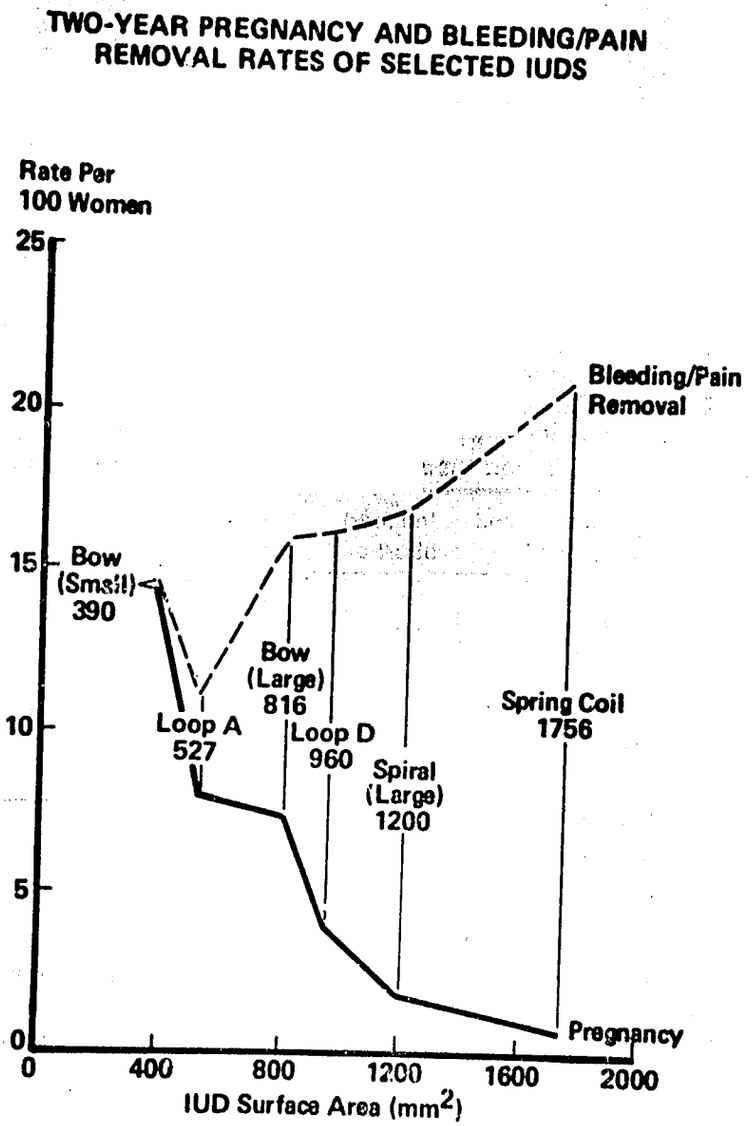

Figure 1. Two-Year Pregnancy and Bleeding/Pain Removal Rates of Some Barium Polyethylene IUDs as a Function of Their Surface Area. (Data from Cooperative Statistical Program of the Population Council and the International Fertility Research Program.)

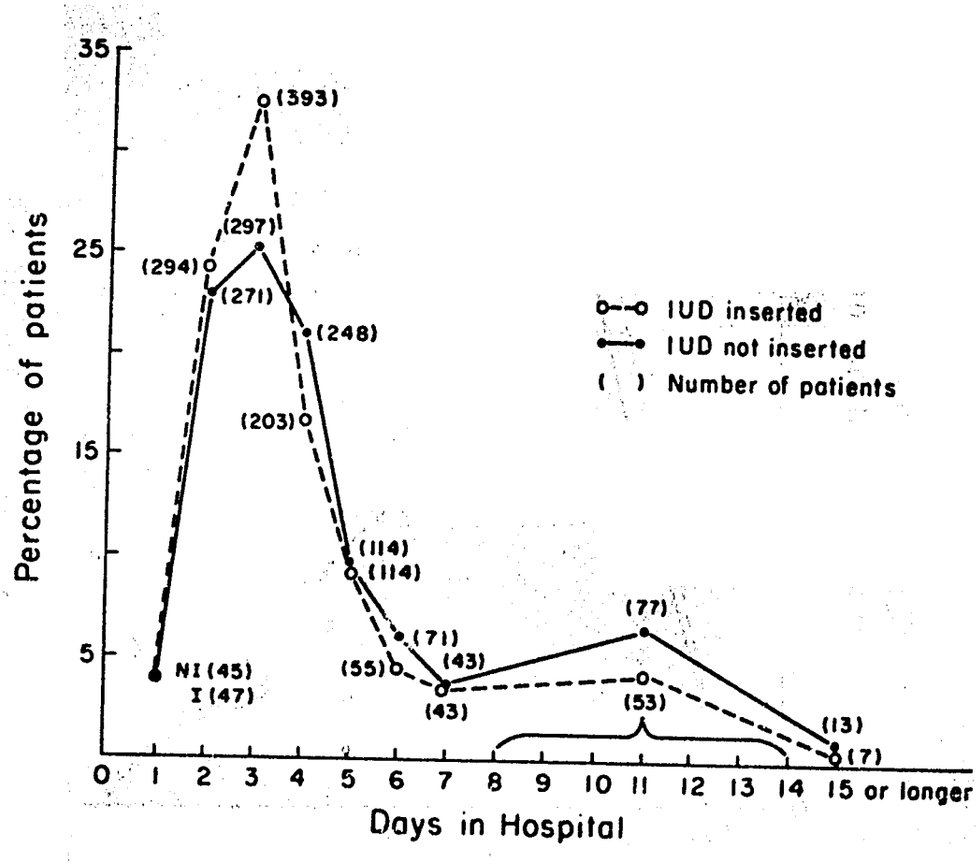

Figure 2. Length of Hospitalization in Patients with Abortions Initiated Out of the Hospital.

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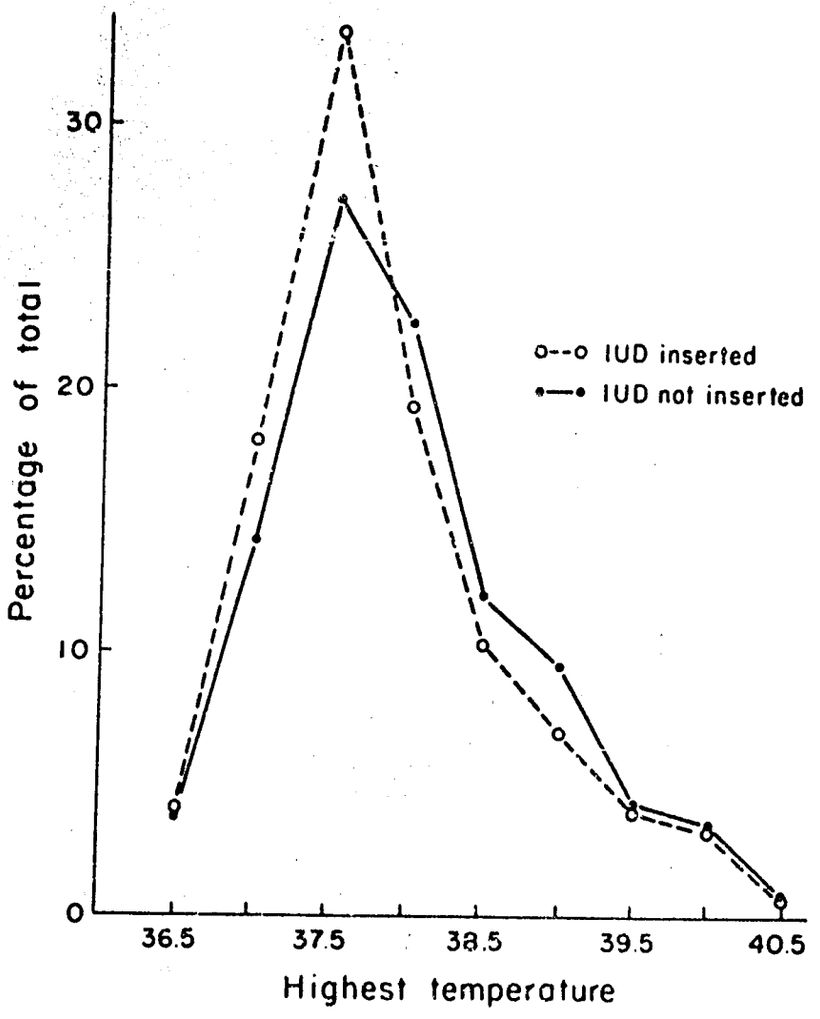

Figure 3. Highest Temperature During Hospitalization (with Antibiotics). Abortions Initiated Out of the Hospital.

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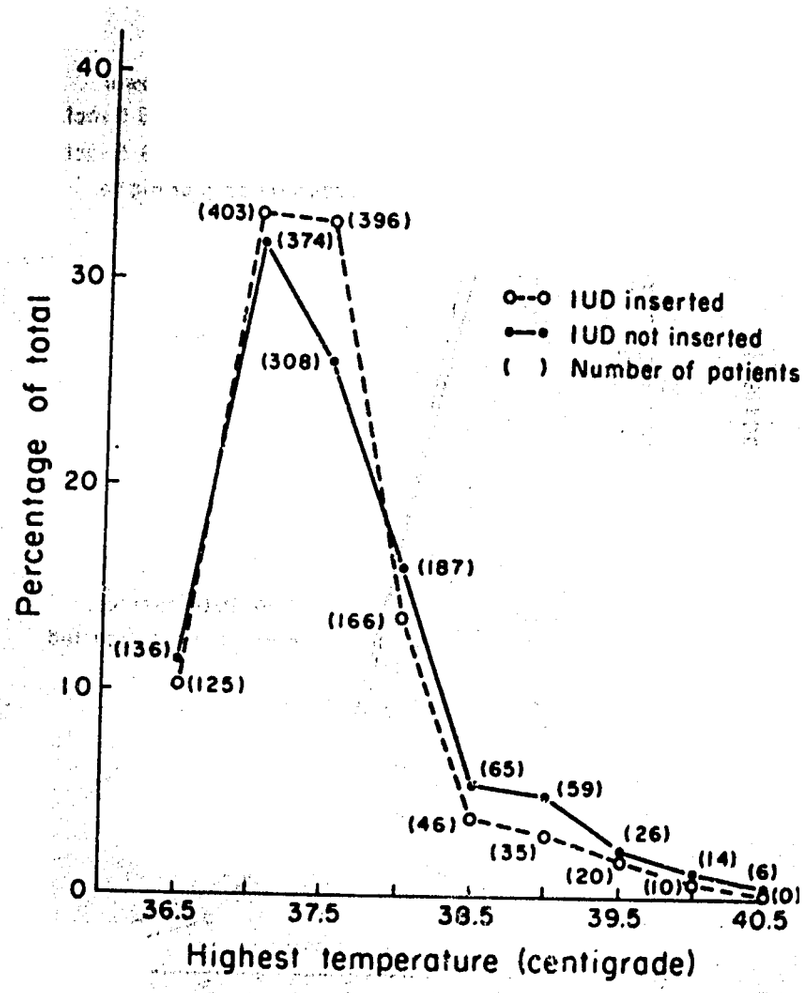

Figure 4. Distribution of Fever For All Patients in Both Groups. Abortions Initiated Out of the Hospital.

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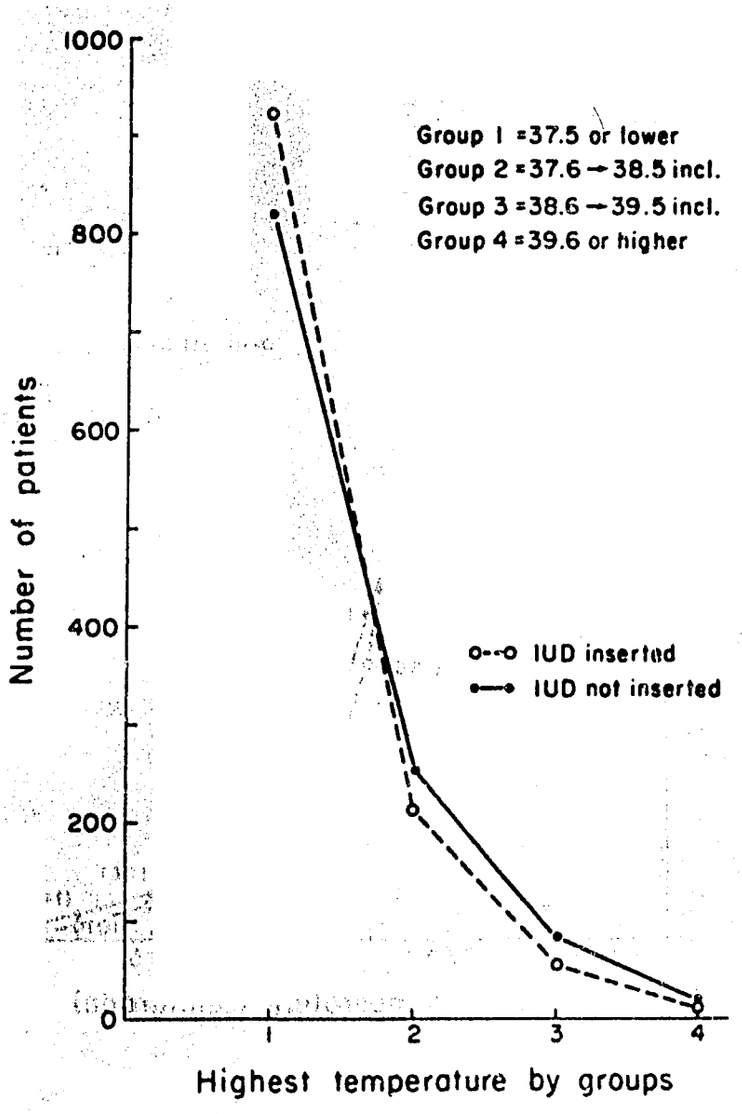

Figure 5. Ranges of Temperature For All Patients of Both Groups. Abortions Initiated Out of the Hospital.

From: Tatum, H J: Intrauterine Contraception. Am J Obstet Gynecol 112(7):1000, 1972.

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THE NEW ENGLAND JOURNAL OF MEDICINE 296 (21): 1236-7, May 26, 1977

INCREASED RISK OF BREAKTHROUGH BLEEDING WHEN ONE ORAL-CONTRACEPTIVE TABLET IS MISSED

To the Editor: Breakthrough bleeding is quite common among users of oral contraceptives and is a frequent reason for discontinuing this method. The incidence of this side effect, however, varies from one study to another. Some of this variation may relate to how regularly the contraceptive tablet is ingested in different study populations. In a double-blind crossover study (480 cases) on the differential effects of three oral contraceptives — Ovral (ethinyl estradiol, 0.05 mg, and norgestrel, 0.5 mg), Norinyl (mestranol, 0.05 mg and norethindrone, 1.0 mg) and Norlestrin (ethinyl estradiol, 0.05 mg, and norethindrone acetate, 1.0 mg) — carried out in Seattle, Washington, on the West Coast of the United States, the effect of missing one contraceptive tablet on breakthrough bleeding was measured by intensive follow-up observation of the study subjects every two weeks. They were instructed to take two contraceptive tablets on the day after they missed a contraceptive tablet. The study population consisted of women 18 to 40 years of age; 90 per cent of the sample population were never married, white and between the ages of 18 and 25 years. Almost all women had 10 or more years of education. Every two weeks women were asked by telephone about various side effects associated with the oral contraceptives one by one and whether they had missed taking any oral-contraceptive tablet. The data were recorded for each day on a daily grid.

For women who took oral-contraceptive tablets each day the probability of breakthrough bleeding on the following day was found to be in the range of 0.017 to 0.022. The comparable probability of breakthrough bleeding on the day after one missed contraceptive tablet was 0.227 to 0.352. (The range reflects differences among the three types of oral contraceptives.) The risk, therefore, of breakthrough bleeding increased 13 to 16 times if one oral-contraceptive tablet was missed. The duration of breakthrough-bleeding episodes, however, among women who bled on the day after a missed contraceptive tablet was two thirds to three fourths as long as that for women who bled without missing a contraceptive tablet. The ranges show differences in the three types of oral contraceptives — namely, Ovral, Norinyl 1/50 and Norlestrin 1.

The increased risk of breakthrough bleeding suggests the importance of taking the pill regularly. Although missing one oral-contraceptive tablet may not appreciably increase risk of pregnancy, it definitely increases risk of breakthrough bleeding to the woman, even if she doubles up the oral contraceptive on the following day. A better regimen might include an instruction to take the oral-contraceptive tablet soon after she remembers, rather than two tablets on the following day.

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Changes in Menstrual Cycle Length and Regularity After Use of Oral Contraceptives

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ABSTRACT

Taylor, R. N., Jr., Berger, G. S. and Treloar, A. E. (International Fertility Research Program, Research Triangle Park, North Carolina and Menstruation and Reproduction History Program, Boynton Health Service, University of Minnesota, Minneapolis, Minnesota, USA). *Changes in menstrual cycle length and regularity after use of oral contraceptives.*
Int J Gynaecol Obstet 15: 55-59, 1977

This is an analysis of changes in menstrual cycle length and regularity occurring for a group of 211 women who had discontinued use of oral contraceptives. The analysis is based on prospectively recorded histories from the Menstruation and Reproduction History Program. Post-pill menstrual cycle length and regularity are compared with pre-pill averages. In the first post-pill cycle, there was an average increase of 6 days in cycle length. In subsequent cycles, however, cycle length and regularity were comparable to pre-pill norms in most cases.

INTRODUCTION

The effects of oral contraceptives on the female reproductive system have been studied extensively during the past 2 decades. One area of concern has been the question of whether suppression of normal hypothalamic-pituitary-ovarian function persists after a woman stops taking the hormonal preparation. Since the pattern of menstrual bleeding is an indirect indication of how this endocrine axis is functioning, various investigators have studied post-pill menstrual patterns and have suggested that women who have irregular menses prior to taking the pill, late menarche, or low body weight are more likely to develop post-pill oligomenorrhea than women without these characteristics (1-3).

The present investigation was undertaken in an effort to determine in more detail the apparent effects of oral contraception on menstrual cycles subsequent to OC use taking into account certain characteristics of the women present before they began using the oral contraceptives.

This paper was presented at the IX World Congress of Fertility and Sterility, Miami Beach, Florida, USA, April 12-16, 1977.

MATERIALS AND METHODS

Selection criteria

From the prospectively recorded histories maintained by the Menstruation and Reproduction History Program of the University of Minnesota, the records of 211 women less than 40 years of age who met the following criteria were selected for analysis:

1. Used and subsequently discontinued OC use during the 5-year study period (1965-1969)
2. Reported the precise dates on which they began using and stopped using OCs
3. Reported withdrawal bleeding after discontinuing the pill
4. Reported the dates of onset of 7 menses preceding pill use and the date of onset of at least the first menstrual period after discontinuing pill use
5. Did not become amenorrheic while using OCs and did not become pregnant until they had at least 1 menstrual period after discontinuing the pill

Subjects

Women aged 40 or over were excluded from the analysis because of the extreme natural variability in their menstrual patterns (4). The age distribution of the cohort showed 91.0% in their 20s, with only 2.6% younger than 20 and 0.9% 35 years or older. More than half (57.2%) were nulliparous, 26.4% were primiparous, and 16.4% were multiparous.

Because of breaks in case histories and pregnancies, 38% of the cohort experienced attrition by the sixth post-pill cycle. The number of women in the cohort for each cycle is given in Table I.

Definitions

To establish a baseline measurement of menstrual patterns prior to OC use, the average menstrual cycle length and an index of irregularity were computed for 6 consecutive pre-pill cycles for each woman. A cycle was defined as the number of days between the onset of 2 consecutive menstrual flows as recorded by the subjects.

The index of irregularity was defined as the average of the absolute difference in length of pairs of consecutive cycles. A zero score on this measure indicates perfect regularity, and large numbers indicate substantial irregularity. For 2 consecutive menstrual cycles, the index of irregularity simply equals their difference in length. For more than 2 cycles, the index describes the average difference between consecutive cycle lengths. Such a measure has the interpretive advantage of approximating the statement of a woman that she menstruates regularly within a given number of days.

Table I. Number of women remaining in the cohort for each post-pill cycle

Cycle	Cases Lost	Cases Remaining
1	0	211
2	18	193
3	16	177
4	20	157
5	16	141
6	11	130

Since the intent of this study was to describe changes in menstrual patterns after OCs were discontinued, the average cycle length before OCs were initiated was subtracted from the length of each of the 6 immediate post-pill cycles. In this way, a measure of the degree of deviation from the pre-pill average length was obtained for each post-pill cycle. This measure indicates the deviation in length from the pre-pill norm for a given post-pill cycle.

A similar procedure was followed in obtaining measures of relative regularity for pairs of consecutive post-pill cycles. The pre-pill average irregularity index was subtracted from the index obtained for each pair of consecutive post-pill cycles. In this way a measure of the difference in regularity from the pre-pill average was obtained for cycles 1 and 2, for cycles 2 and 3, and so on.

RESULTS

Post-pill cycle length

Fig. 1 describes the differences between post-pill cycle lengths and the pre-pill average for the cohort for the first 6 cycles following OC discontinuation. This series of histograms indicates that the first post-pill cycle was longer than the pre-pill average for the majority of cases. The histograms for cycles 2 through 6 display a modal category of women with less than 2 days difference between pre- and post-pill cycle lengths. The distributions appear roughly symmetrical by the second cycle, since approximately the same proportion of women have shorter cycles as have longer cycles. As the length of time from pill discontinuation increases, a trend toward cycle lengths shorter than the pre-pill average is established.

Fig. 2 presents the median difference between mean pre-pill cycle lengths and each post-pill cycle. For the median case, the first cycle was 6 days longer than the pre-pill average. By the second cycle, the median was shorter than the pre-pill average and tended to remain at or below the pre-pill average through the sixth cycle.

Post-pill regularity

Fig. 3 displays the frequency distributions of differences between the pre-pill average irregularity index and the irregularity of each pair of consecutive post-pill cycles. The pattern is very similar to that exhibited by the distributions of cycle length differences. Cycles 1 and 2 are relatively irregular, with the median case being 3 days less regular than the pre-pill average (Fig. 4). This is due, no doubt, to the extended length of the first cycle noted previously.

The distributions of the remaining consecutive cycle pairs exhibit a gradual trend toward re-establishing the pre-pill degree of regularity. By cycles 3 and 4, half the women menstruated within 2 days of their pre-pill average irregularity; a little more than one quarter had become more regular by 2 days or more; and slightly less than one quarter had become less regular by 2 days or more. The index of irregularity of the median case fell to the pre-pill average at cycles 4 and 5 and was 0.4 days more regular at cycles 5 and 6.

Correlation with hypothesized risk factors

In order to evaluate the validity of various risk factors for post-pill amenorrhea and oligomenorrhea, 2 predictive models were constructed, using multiple regression techniques. The first model accounted for 76% of the variance of the length of the first post-pill menstrual cycle, using the average pre-pill cycle length, average pre-pill index of irregularity, age, parity, age at menarche, and the length of the menstrual cycle immediately preceding contraceptive use. The second model explained 75% of the variance of the average index of irregularity over the 6 cycles following pill discontinuation with the same risk factors. Of the various factors, the length of the pre-pill cycle was the most predictive single factor for post-pill cycle length and regularity, explaining 55% and 38% of the variance, respectively.

DISCUSSION

Because the length of the menstrual cycle is highly variable and cycle patterns tend to be unique for

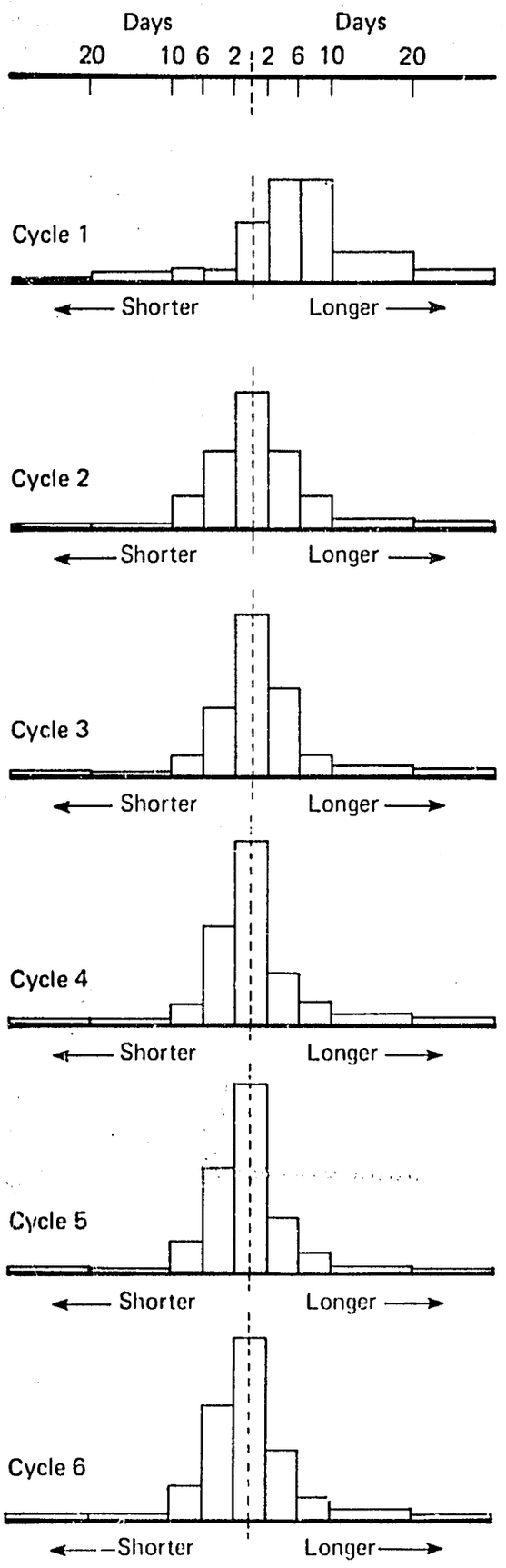

Fig. 1. Differences in length between pre-pill average and post-pill cycles.

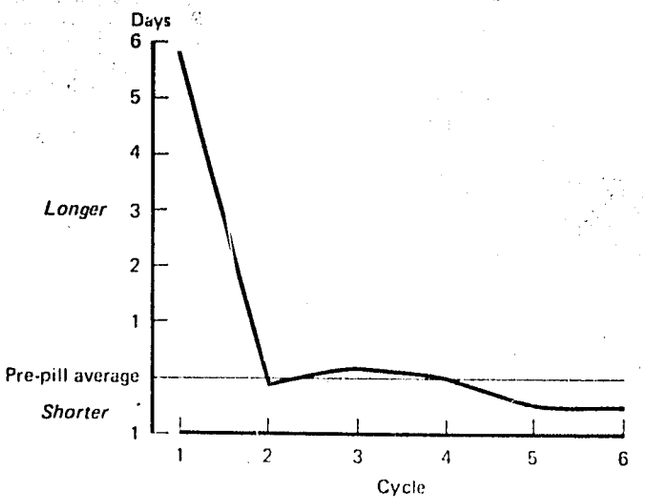

Fig. 2. Median difference in length between pre-pill average and post-pill cycles.

individuals (5), accurate study of menstrual cycle patterns after use of oral contraception must take into account the pre-pill patterns of the individuals under study.

The data on menstrual events used in this study were recorded as the events occurred; thus, the results are not subject to the potential biases inherent in studies based on recalled experience. While our results are consistent with earlier reports that some women develop "more irregular" menstrual patterns after oral contraceptive use, it is apparent from the distributions of observations that the marked shift toward less regularity in the first post-pill cycle disappears by the third post-pill cycle and that approximately as many women become more regular as become more irregular in comparison to the average of the 6 cycles preceding OC use. Similarly, in the first post-pill cycle, a significant increase in cycle length is observed for a majority of the women, but by the second or third post-pill cycle, the proportion of women with shorter cycle lengths approximates those with longer cycle lengths. By the sixth post-pill cycle, there appears to be a trend toward slightly shorter, more regular cycles, but this may simply reflect the known effect of aging on menstrual regularity in these age groups rather than any long-term effect of the oral contraceptives.

Because of the concern about "oversuppression" of the hypothalamic-pituitary-ovarian axis associated with OC use, it is generally regarded as good medical practice to caution women with oligomenorrhea or highly irregular menstrual periods that they may be at particular risk of prolonged amenorrhea and possibly anovulation after using OCs. Our models confirm that the length and regularity of the menstrual cycle prior to initiating use of OCs are highly predictive of the length and regularity of cycles after OC use. However,

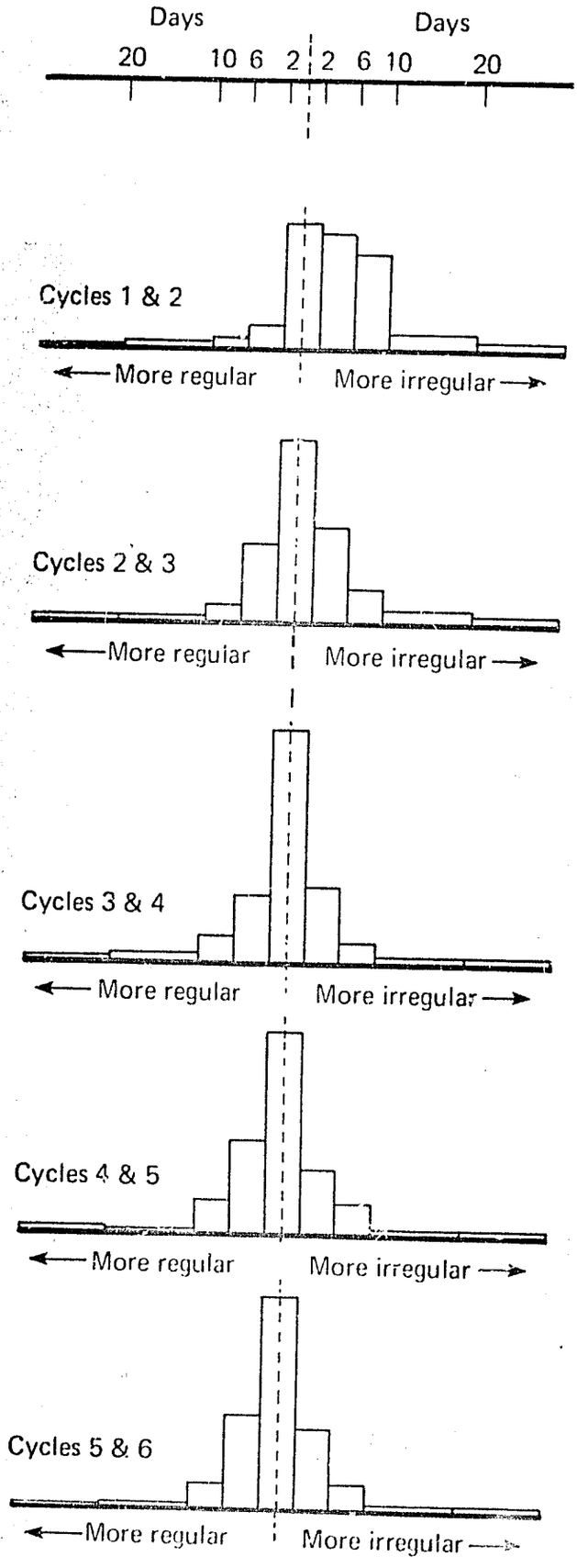

Fig. 3. Difference in regularity between pre-pill average and successive post-pill cycle pairs.

since the menstrual patterns of these women are highly variable to begin with, it is not clear to what extent administering oral contraceptives may be a causal or a contributory factor in the observe post-pill menstrual irregularity. Regardless of the effect on menstruation, there is some evidence, first reported in 1970 by Wolfers (6), of a short delay in return to maximum fertility after OC use. The large prospective study of the Royal College of General Practitioners confirmed that while there is a 2- to 3-month lag before expected rates of fertility return there is no significant difference in fertility rates between prior OC users and nonusers after this time (4).

Clinicians must always keep in mind the potential long-lasting effects of oral contraceptives on reproductive function. However, based on the present analysis, it remains questionable to what extent the pill plays a contributory role in menstrual dysfunction. It is clear from the present study that women who have lengthy or irregular periods before taking oral contraceptives are most likely to experience prolonged and/or irregular cycles after discontinuing the contraceptive medication. Continued long-term follow-up of women in this study is planned to document their future reproductive histories in comparison to those women who have never used steroidal contraceptives.

ACKNOWLEDGMENT

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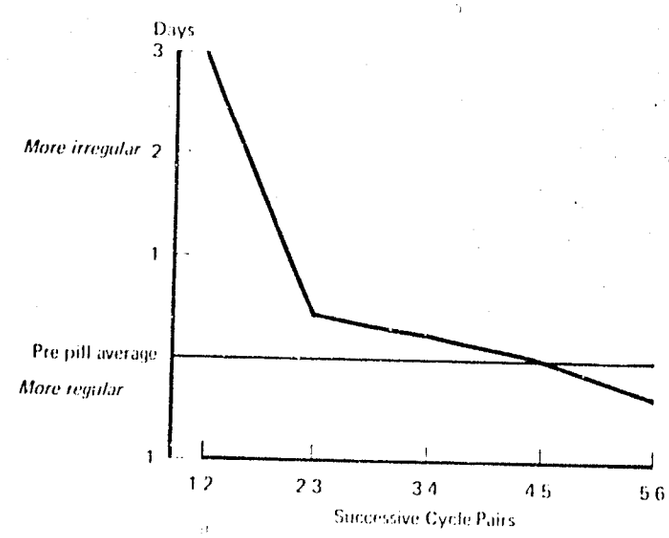

Fig. 4. Median difference in regularity between pre-pill average and successive post-pill cycle pairs.

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ORAL CONTRACEPTIVE POTENCIES AND SIDE EFFECTS: A RANDOMIZED, DOUBLE BLIND STUDY OF OVRAL, NORINYL 1/50 AND NORLESTRIN 1 MG

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Abstract

ORAL CONTRACEPTIVE POTENCIES AND SIDE EFFECTS:
A RANDOMIZED, DOUBLE BLIND STUDY OF OVRAL,
NORINYL 1/50 AND NORLESTRIN 1 MG

Gary S. Berger, MD, MSPH
Prem P. Talwar, PhD

A set of empirical results is used to test a model that assigns rankings to oral contraceptives in terms of relative hormonal potencies. The association between observed incidence of side effects attributed to excess of estrogen and progestin and their incidence as predicted by the model is analyzed. Results of the study show the model to have incorrectly predicted the observed ranking order of symptoms associated with excess estrogen. Further, while the model correctly predicted the oral contraceptive with the highest progestogenic potency (Ovral), the observed ranking order of the other two preparations is shown to be the reverse of that predicted by the model.

I. INTRODUCTION

There is a large variety of oral contraceptives (OC) available for prescription in the United States. Selecting the "optimum" product for a particular patient is a concept which has been promoted in drug advertisements. Some authors have expressed the belief that, based on various characteristics of the woman, one can select a specific product from the spectrum of agents available which will be most likely to avoid side effects or modify ones experienced while taking another preparation (1-3). Such an approach requires categorizing the different OC preparations according to the relative potencies of their hormonal components.

The effort to rank contraceptive products in terms of relative potencies and predicted side effects has been based partly on experimental observations in laboratory animals and partly on clinical observations. However, because the occurrence and reporting of specific side effects is extremely variable in different study populations, it has been difficult to test the models of relative potencies which have been proposed. The present randomized double blind study was undertaken in an attempt to correlate the reported incidence of side effects associated with three different contraceptive preparations, with the incidence predicted by a standard model of predicted relative estrogenic and progestogenic potencies.

II. MATERIAL AND METHODS

In a prospective double blind study carried out at the Planned Parenthood Clinic, in Seattle, Washington, 480 healthy women who had not used any steroidal contraceptives in the preceding three months and who desired oral contraception were randomly assigned Ovral, Norinyl, or Norlestrin*. As previously reported, the women in these three OC groups were similar with respect to a number of socio-demographic and obstetric characteristics (4).

Every two weeks, a public health nurse telephoned each study patient to ask whether she had experienced any symptoms related to the use of the OC since the last contact. To help the patient recall pertinent events, the interviewer would ask the subject about each of 27 symptoms or complications according to a standard protocol. The present analysis is based on those symptoms which are attributed to excess or deficiency of estrogen and progestin as presented by Dickey (2). A listing of the specific symptoms analyzed in the study and those which could be classified in the categories of estrogen excess and progestin excess are listed in Table I. Other symptoms which did not meet the classification criteria were excluded.

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*The estrogen-progesterone composition of Ovral (Wyeth) is ethinyl estradiol 0.05 mg and dl-norgestrel 0.5 mg; Norinyl (Syntex) is mestranol 0.05 mg and norethindrone 1.0 mg; and Norlestrin (Parke Davis) is ethinyl estradiol 0.05 mg and norethindrone acetate 1.0 mg.

Previous study has shown that women are most likely to experience side effects of OCs during the first cycle of OC use. Therefore, each of the three oral contraceptives was ranked according to the incidence rates in the first cycle of use on the specific symptoms associated with excess or deficiency of the hormonal component in the pill. The observed rankings were then compared with those expected on the basis of the model (2); the expected ranking of the three OCs under study was Norlestrin, Norinyl, and Ovral for decreasing estrogenic potency and Ovral, Norlestrin, and Norinyl for decreasing progestational potency. Friedman's two-way analysis of variance on ranks (5) was used to test similarities in the ranks of incidence rates of the three OCs on each specific symptom.

III. RESULTS

The observed incidence rates during the first cycle of OC use for all symptoms attributable to excess of estrogen are shown in Table II. Across the top row, the three OCs are listed in the order which would be expected from Table II. Ranking of the three OCs in order of frequency of each side effect did not show any pattern significantly different from random variation ($.30 \leq P \leq .40$, Friedman's statistics).

The observed incidence rates of symptoms for each of the three OCs attributed to progestin excess are shown in Table III. The three OCs are again listed across the top row in the expected order. The test statistics on ranks show that Ovral users, as expected from the model, have a significantly ($.01 \leq P \leq .05$) higher incidence of symptoms, but Norinyl users more frequently reported symptoms of progestin excess than Norlestrin-- a result which is opposite to that predicted by the model.

Because of the small number of reports in our data on symptoms attributed to deficiency of either estrogen or progestin, we were unable to compare ranks of incidence rates for these categories.

IV. DISCUSSION

Because of the different combinations of type and dose of the progestins and estrogens used in the contraceptive pills now available, predictions of relative potencies based on animal assays and steroid content may lead to erroneous conclusions about the clinical effect of one pill compared to another. One limitation of previous studies of incidence rates of side effects of various contraceptive preparations is the lack of random allocation of subjects to the various contraceptives being compared. Without such random allocation, it is difficult to determine whether different rates of side

effects are actually related to the different hormonal preparations. The present study, however, has the advantage of being conducted in a randomized, double blind fashion.

On the basis of the etiologic classification of side effects given in Table I, each of the three OCs tested (Norinyl 1/50, Norlestrin 1 mg, and Ovral) was ranked according to the observed order of incidence rates of side effects attributed to estrogen or progestin excess and these rankings were then compared with those expected on the basis of the model proposed by Dickey. This model was not found to be predictive of the rank order of symptoms associated with excess estrogen. Furthermore, although the model did predict correctly the OC with the highest progestogenic potency (Ovral) it did not predict the correct order of frequency of side effects attributed to excess progestin for Norinyl and Norlestrin. Recently, data from the Royal College of General Practitioners' Study suggests an association between hypertension and progestin content, rather than estrogen as in the present model (6). Even taking this reclassification into account, the results of the present study remain essentially the same.

Our failure to confirm Dickey's clinical model may have been caused by the fact that the three OCs tested were close in the ranks for estrogenic and progestin potencies. This analysis should,

therefore, be taken as only a preliminary test of the clinical model. At present, our opinion lies in the middle road between the belief that side effects can be predicted from a model of drug potencies and the opinion expressed by Edgren and Sturtevant that, "no laboratory or clinical measures of potency will predict specific side effects with useful precision (7)."

The present results do suggest a need for continued gathering of comparative data on side effects of various contraceptive pills in efforts to identify real differences. Such studies will be helpful in making the most appropriate choice of OC at the time of initiation and/or at the time of changing an OC if some side effects persist.

Nonproprietary Names
and Trademarks of Drugs

ethinyl estradiol and dl-norgestrel -- Ovral
mestranol and norethindrone -- Norinyl
ethinyl estradiol and norethindrone acetate -- Norlestrin

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TABLE I
CLASSIFICATION OF ORAL CONTRACEPTIVE SIDE EFFECTS CAUSED BY AN EXCESS OF ESTROGEN AND PROGESTIN*

ESTROGEN EXCESS	PROGESTIN EXCESS
Vascular headache	Fatigue
Hypertension	Depression
Nausea	Decreased libido
Vomiting	Increased libido
Dizziness	Days of flow
Leg Cramps	Increased appetite
Irritability	Acne
Bloating	Rashes

** Abstracted from Table III in Reference 2 for the symptoms pertinent to this study.*

TABLE II

RANKS DURING THE FIRST CYCLE OF USE OF ORAL CONTRACEPTIVES FOR SYMPTOMS RELATED TO ESTROGEN EXCESS LISTED IN ORDER PREDICTED BY CLINICAL MODEL*

Symptom	Predicted Rank		
	–1– Norlestrin	–2– Norinyl	–3– Ovral
	Observed Rank		
Headache	3(29.5)**	1(34.5)	2(32.9)
Nausea	2(45.9)	3(38.5)	1(49.6)
Vomiting	1(13.0)	2(8.7)	3(7.2)
Dizziness	2(8.9)	3(8.7)	1(13.2)
Leg cramps	3(11.0)	2(11.4)	1(14.5)
Abdominal bloating	1(41.1)	2(37.6)	3(31.6)
Irritability	3(24.7)	2(29.5)	1(31.6)
Hypertension			
Systolic (BP ≥ 140)	2(2.7)	3(1.0)	1(3.9)
Diastolic (BP ≥ 90)	1(4.5)	3(1.0)	2(1.9)

* *Table XIII in Reference 2.*

** *Figures in parentheses are the incidence rates (%).*

TABLE III

RANKS DURING THE FIRST CYCLE OF USE OF ORAL CONTRACEPTIVES FOR SYMPTOMS RELATED TO PROGESTIN EXCESS LISTED IN ORDER PREDICTED BY CLINICAL MODEL*

Symptom	Predicted Rank		
	—1— Ovral	—2— Norlestrin	—3— Norinyl
	Observed Rank		
Fatigue	1(30.9)**	3(25.3)	2(29.5)
Depression	1(32.9)	3(26.7)	2(31.6)
Decreased libido	3(2.0)	2(4.8)	1(10.1)
Increased libido	1(18.0)	3(14.4)	2(16.1)
Days of flow	=(3.8)	=(3.8)	=(3.8)
Increased appetite	1(33.6)	3(26.7)	2(30.3)
Acne	1(43.9)	3(38.4)	2(42.3)
Rashes	1(13.2)	3(7.5)	2(11.4)

* *Table XIII in Reference 2.*
** *Figures in parentheses are incidence rates (%).*

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AN APPROACH TO QUANTIFYING BREAKTHROUGH BLEEDING IN ORAL CONTRACEPTIVE STUDIES

Prem P. Talwar, International Fertility Research Program

INTRODUCTION

Breakthrough bleeding has been reported as one of the important causes of dissatisfaction with fertility control methods. Its importance was amply indicated when the WHO Task Force on Acceptability of Fertility Regulating Methods recommended at its 1973 meeting that multinational social science research be initiated on patterns and perceptions of menstrual bleeding (1). Although the methodology and approaches adopted differ from one study to another, every study of contraceptive methods, especially those concerning IUDs and steroidal contraceptives, has described the phenomenon of bleeding associated with the contraception. In some studies, the bleeding is described quantitatively by indices such as the percentage of women reporting the symptoms, or the number of days or number of episodes of bleeding, or by more than one of these indices. In other studies, women are asked to report subjectively whether "increase", "decrease" or "no change" occurs in menstrual bleeding when the period of contraceptive use is compared to the period of precontraception (2,3,4,5). These different approaches in analysis, in addition to differences in the design of the study and conceptual definitions, have made it difficult, if not impossible, to compare results of different studies. In 1976, Rodriguez attempted to standardize the definitions and the method of analysis of the menstrual patterns (6). In a later workshop, problems related to the study of menstrual patterns were discussed more thoroughly, and most of the recommendations made by Rodriguez were accepted with or without modifications (7).

The framework of standardized methodology (6, 7) is more appropriate when the contraceptive method under study tends to disrupt the menstrual cycle completely. In that situation, the use of indices showing only bleeding episodes (which includes all types of bleeding--menstrual or intermenstrual) is valid. But with oral contraceptives (OCs), there are two distinct types of bleeding which occur cyclically; combining the two and ignoring their distinctiveness can in no way be justified. Equating the effects of one episode of breakthrough bleeding with withdrawal bleeding on acceptability and continuation is not only undesirable, but also objectionable. Moreover, there is a definite need for treating each contraceptive cycle, especially the earlier ones, separately because of (a) evidence of a stabilization trend in breakthrough bleeding during the use of the first few contraceptive cycles, and (b) higher differences in the incidence of breakthrough bleeding among different OCs during the first and second cycles of use (2). Therefore, it is recommended that for the study of oral and other contraceptives which have cyclical patterns of bleeding, a reference period should consist of one contraceptive cycle rather than a period of 60 or 90 days (6,7).

This paper presents an approach, differing from that of Rodriguez, for quantifying breakthrough bleeding in oral contraceptive users. A method of computing an index of breakthrough bleeding is discussed which not only can be used to compare bleeding patterns of different OCs but is also useful to relate this symptom to a woman's medical, physiological, and biological profile. It is assumed that there are two main dimensions of this symptom, namely, persistence and severity (Snowden, reference 7, has described them by duration of bleeding and volume of blood loss), and each dimension has more than one level. Thus, a multivariate observation consisting of two levels of persistence (number of days of bleeding and number of episodes of bleeding in a contraceptive cycle) and three levels of severity (spotting, and light and heavy bleeding) describes the breakthrough bleeding pattern of a woman. Three severity levels of bleeding have been considered instead of two (considered in references 6 and 7) because of the different effects they may have on acceptability and continuation rates. These three levels can be suitably defined or modified to reflect the degree of dissatisfaction in the cultural context of the country. This six-variate information was converted to a composite index because any index based on one of the variates was not found to be comprehensive enough to include information on all aspects of bleeding. The composite index thus derived was used to study differential patterns of breakthrough bleeding for three groups of women using Ovral (ethinyl estradiol 0.05 mg and dl-norgestrel 0.5 mg), Norinyl (mestranol 0.05 mg and norethindrone 1.0 mg), and Norlestrin (ethinyl estradiol 0.05 mg and norethindrone acetate 1.0 mg).

MATERIALS AND METHOD

The data were obtained in a double-blind comparative study on Ovral, Norinyl and Norlestrin carried out in 1974 at the Planned Parenthood Clinic of Seattle, Washington. A sample of 480 women who had no contraindications for OC use, including no irregularities in their menstrual cycles, and who had not used steroidal contraceptives in the preceding three months were randomly assigned to one of these study OCs and given three cycles of supply, each containing 21 hormonal and seven placebo tablets. Information on 27 symptoms associated with OC use was collected by a public health nurse who telephoned each subject every two weeks to ask whether she had experienced any symptom (which women associate with OC use) since her last contact. Inquiry was made about each such symptom in order to ensure the reporting of all pertinent events, and the information was recorded on a symptom grid by the day on which symptoms appeared (2).

Only the information on intermenstrual vaginal bleeding during the period hormonal pills were taken in the first cycle of OC use was

utilized in the analysis. Questions were asked about the day when breakthrough spotting or bleeding occurred, whether protection by tampons or pads was required, and in what quantity. Events of breakthrough bleeding were defined in this study as spotting, when no protection was needed; light bleeding, requiring one pad a day; and heavy bleeding, when two or more pads were used. Future studies may alter these definitions, when appropriate, to reflect the degree of dissatisfaction in the cultural context of the population under study.

The choice of a composite index based on both the dimensions of breakthrough bleeding was made because of its comprehensiveness in covering information on all aspects of bleeding; this is not possible if one or more levels of one dimension is used as an index (Table I). The first component of the Principal Component Analysis was used as an index. Because more than one such index can be obtained by adopting variations of the Frincipal Component technique on the same set of variables or by using different subsets of the variables, a choice of the "best" index was made based on the degree of information on different aspects of breakthrough bleeding contained in the index. (Eigenvectors vary by the choice of the matrix used to extract eigenvalues. Variance-Covariance matrix gives a set of eigenvectors different from the ones obtained from the correlation matrix.)

DEVELOPING AN INDEX TO QUANTIFY BREAKTHROUGH BLEEDING

Choice of variables

The combinations of two levels of persistence and three levels of severity resulted in the following six variables (X_1, $X_2 \ldots X_6$) which cover most of the information on breakthrough bleeding on an individual woman:

$X_{1(2,3)}$ = Number of days of spotting (light bleeding, heavy bleeding)

$X_{4(5,6)}$ = Number of episodes of spotting (light bleeding, heavy bleeding)

Because the first set of three variables are different in measurement units from the second, it was desirable either to convert them into comparable units or make them unitless (dimensionless) so that they might be combined into one index. For this purpose, the observed measurements (X's) were converted to percentages (P's) by relating them to the overall value for the population. (Because the purpose was to obtain dimensionless variables, any average value could have served.) That is, the new variables P_i's were obtained in the following fashion:

$$P_i = [X_i / X_i(A)] \times 100$$

Where:

X_i = observed value of the ith variable

$X_i(A)$ = average value of X_i $\left(\frac{\sum_{j=1}^{n} x_{ij}}{n}\right)$,

where n is the number of women on whom the information on the X_i variable was available

Thus, the redefined six-variate information for women used in the development of the index is:

$P_{1(2,3)}$ = Number of days of spotting (light or heavy bleeding) for a woman as the percentage of the average number of days of spotting (light or heavy bleeding) in the population under study

$P_{4(5,6)}$ = Number of episodes of spotting (light or heavy bleeding) for a woman as the percentage of the average number of episodes of spotting (light or heavy bleeding) in the population

Choice of several indices

Once these variables were made dimensionless, the next step was to look for a comprehensive index which includes the most information contained in the six variables. The first consideration was whether one of the variables could serve as the index. To test it, a correlation matrix consisting of correlation coefficients between different P's was computed. It may be seen (Table I) that a single variable is not sufficient to be an index because it does not contain information on the other variables. Thus, a need for a composite index was indicated. The first component of the Principal Component Technique on the six-dimensional vector ($P_1, P_2 \ldots P_6$) is a valid index, often used by statisticians to represent a multivariate observation more parsimoniously (8, 9, 10). Geometrically, this index is a linear combination of the variables which cover the maximum variance in the sample scatter configuration. For computations, BMD computer programs prepared by the University of California, Los Angeles, were used (10). The first principal component was obtained by deriving the weights from the eigenvector corresponding to the largest eigenvalue of the variance-covariance or correlation matrix of the multivariate observations. The breakthrough bleeding score for an individual was then obtained from the product of the vector of the standardized variables and the eigenvector. That is, if ($b_1, b_2 \ldots b_k \ldots$) is an eigenvector corresponding to the largest eigenvalue, the breakthrough bleeding score for the individual is obtained as

$$\frac{b_1(P_{i1}-\bar{P}_1)}{\sigma_{P_1}} + \frac{b_2(P_{i2}-\bar{P}_2)}{\sigma_{P_2}} + \ldots + \frac{b_k(P_{ik}-\bar{P}_k)}{\sigma_{P_k}} + \ldots$$

where σ_{P_k} is the standard deviation for variable P_k, P_{ik} is the observed measurement (as derived for this study), and $\bar{P}_k$ is the mean measurement of the variable P_k. Two modifications were done to derive scores for this analysis.

Table I

CORRELATION COEFFICIENTS BETWEEN DIFFERENT VARIABLES AND INDICES

Variables & Indices	Variables P_1	P_2	P_3	P_4	P_5	P_6
P_1	1.000					
P_2	0.073	1.000				
P_3	-0.055	0.141	1.000			
P_4	0.744	0.125	-0.045	1.000		
P_5	0.104	0.707	0.123	0.197	1.000	
P_6	0.0002	0.184	0.820	-0.009	0.227	1.000
I_1	0.6850	0.656	0.198	0.718	0.681	0.305
I_2	0.317	0.693	0.595	0.369	0.733	0.688
I_3	0.125	0.695	0.778	0.062	0.513	0.635
I_4	0.303	0.576	0.430	0.445	0.811	0.659

(1) The scores were approximated as

$$\frac{b_1}{\sigma_{P_1}}(P_{i1}) + \frac{b_2}{\sigma_{P_2}}(P_{i2}) + \ldots + \frac{b_k}{\sigma_{P_k}}(P_{ik}) + \ldots$$

and

(2) $\left(\frac{b_1}{\sigma_{P_1}}, \frac{b_2}{\sigma_{P_2}}, \ldots\right)$ were so chosen that

$$\sum_k \left(\frac{b_k}{\sigma_{P_k}}\right) = 1$$

These two modifications were advantageous in that a woman whose breakthrough bleeding measurements for all six variables were equal to the average in the sample, would score 100.

Using this method, several indices could be developed from the six-variate information on breakthrough bleeding. This was done in two stages. In the first stage, two indices were developed by introducing slight variation in the Principal Component Technique--one of them used a variance-covariance matrix of the six variates to extract eigenvalues and eigenvector and the other used the correlation matrix. As we will see in the next section, the index corresponding to the correlation matrix was found to be better. Thus, in the next stage, correlation matrix was used to extract the eigenvectors. In this stage an attempt was made to determine whether all six variables were needed or whether a subset of them, either P_1 to P_3 or P_4 to P_6, could by itself lead to an index as good as the one based on P_1 to P_6. Thus, two more indices were computed, one based on (P_1, P_2, and P_3) and the other on (P_4, P_5, and P_6).

Choice of the "best" index of breakthrough bleeding

The "best" index is the one which contains most of the information on breakthrough bleeding available in each of the six variates (P_1, $P_2 \ldots P_6$). The operational meaning of this definition is that the index which has the maximum correlation with the individual variable $P_1, P_2 \ldots P_6$ will be the "best". Four indexes considered for the selection of the "best" were the following:

I_1: Index based on (P_1, $P_2 \ldots P_6$), eigenvector obtained from the variance-covariance matrix of the six variables

I_2: Index based on ($P_1, P_2 \ldots P_6$), eigenvector obtained from the correlation matrix of the six variables

I_3: Index based on (P_1, P_2, P_3), eigenvector obtained from the correlation matrix of the three variables

I_4: Index based on (P_4, P_5, P_6), eigenvector obtained from the correlation matrix of the three variables

The correlation coefficients between these indices and the individual variables (P_1, P_2, $\ldots P_6$) are shown in Table I. I_3 has very low correlation with P_1 and P_4 and thus can be omitted when compared to others. Between I_2 and I_4, I_2 is preferred for higher correlation with most of the variables P_1 to P_6, though I_4 has higher correlation coefficients with P_4 and P_5. I_2 is to be preferred over I_1 because of (1) overall higher correlation with all variables P_1 to P_6 and (2) higher correlation with the heavy breakthrough bleeding (variables P_3 and P_6), a more serious side effect. Thus I_2, the "best" index of breakthrough bleeding, is given by

$$I = 0.0676P_1 + 0.163P_2 + 0.200P_3 + 0.104P_4 + 0.205P_5 + 0.255P_6$$

The order of the magnitude of weights may be noted--variables corresponding to heavy bleeding get more weight than those corresponding to

Table II

DISTRIBUTION OF WOMEN USING OVRAL, NORINYL AND NORLESTRIN BY THE BREAKTHROUGH BLEEDING SCORE

Breakthrough Bleeding Score	Types of Oral Contraceptives		
	Ovral (%)	Norinyl (%)	Norlestrin (%)
0	128 (90.1)	72 (51.4)	66 (47.8)
0-10.0	2 (1.4)	3 (2.1)	3 (2.2)
10.0-20.0	5 (3.5)	8 (5.7)	7 (5.1)
20.0-30.0	4 (2.8)	20 (14.3)	20 (14.5)
30.0-40.0	1 (0.7)	9 (6.4)	9 (6.5)
40.0-50.0	0 (0.0)	6 (4.3)	7 (5.1)
50.0-60.0	0 (0.0)	8 (5.7)	8 (5.8)
60.0-70.0	0 (0.0)	4 (2.9)	8 (5.8)
70.0-80.0	1 (0.7)	1 (0.7)	3 (2.2)
80.0-100.0	1 (0.7)	3 (2.1)	4 (2.9)
Over 100.0	0 (0.0)	6 (4.3)	3 (2.2)
Mean Score (all users)	2.7	20.9	22.6
Mean Score (breakthrough bleeders)	27.5	43.0	43.4

light bleeding which, in turn, get more weight than those for spotting. Also, those corresponding to number of episodes are relatively more important than those related to total number of days.

APPLICATION

This index was used to obtain breakthrough bleeding scores for 480 women using Ovral, Norinyl, and Norlestrin in the Seattle study. The distribution of women by their scores and mean scores is given in Table II. The distribution of breakthrough bleeding scores for Ovral users was significantly different ($P<0.01$) from the similar distributions exhibited by Norinyl and Norlestrin users.

SUMMARY AND DISCUSSION

The usual indices of breakthrough bleeding, such as the percent of women reporting breakthrough bleeding and the duration or the number of episodes of bleeding, are not adequate to quantify breakthrough bleeding associated with OC use because they do not contain information on all aspects of bleeding. A composite index was therefore developed by using information on two levels of persistence and three levels of severity of breakthrough bleeding. It was found that more severe bleeding and more frequent episodes of bleeding (rather than days of bleeding) had higher weights in the index. This index was used to quantify breakthrough bleeding scores for women using Ovral, Norinyl, and Norlestrin; Ovral users had significantly different patterns, compared to Norinyl and Norlestrin users whose patterns were similar to each other.

Because breakthrough bleeding is an important factor contributing to dissatisfaction among OC users, it is recommended that more detailed data be collected to develop the composite index. The Principal Component Technique may be used to determine the coefficients of a linear combination of the variables because the coefficients may differ from one population to the other. Such an index can assign scores to individual women; the next step is to identify some medical, physiological, and biological variables which are positively associated with these scores. Such investigation will be helpful in better education and management of the OC acceptors.

Although the index developed here has been discussed in the context of oral contraceptive use, the technique is quite general and can be used for measuring breakthrough bleeding in any setting. It is generally applicable in any situation where multivariate data are to be presented in fewer dimensions to make them more comprehensible.

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Progestagen-only oral contraceptive for breast-feeding women

It is frequently stated that combined oral contraceptives should be avoided by the breast-feeding woman because of adverse effects on the quantity and quality of milk, but that the progestagen-only Pill (" mini-pill ") has less or no effect on lactation and is therefore more desirable for the lactating woman who wants to use oral contraception. This viewpoint was recently supported in the short report in the *IPPF Medical Bulletin* of a meeting on the regulation of fertility during human lactation sponsored by the International Planned Parenthood Federation.[1]

However, it should be realized that such a general statement needs qualification, since different progestagens vary with respect to their oestrogenic, progestational, and androgenic effects and, therefore, one might expect varying effects on lactation. The literature supports this view. It has been reported that megestrol acetate, 0·5 mg daily or chlormadinone acetate, 0·5 mg daily, do not affect lactation,[2] but daily administration of norethisterone, 0·35 mg, has been found to decrease the quantity and quality of human milk.[3] The differences could be related to the fact that the former two compounds belong to the 17-α-hydroxyprogesterone group and have no oestrogen effect, while norethisterone, belonging to the 19-nortestosterone group, has mild androgenic effects.

In contrast to the current blanket recommendation that the progestagen-only Pill is suitable for lactating women, we believe it essential to qualify this statement by indicating the specific compounds and dosages of the progestagen-only Pill. This would require that the pharmacology of all available progestagen-only oral contraceptives be studied for their oestrogenicity and androgenicity, and the one with least potency in either respect be recommended to lactating mothers. Such analysis and communication of the result to the general clinician and practitioner will be helpful for better management of contraception among lactating mothers.

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THE RISKS AND BENEFITS OF HORMONAL CONTRACEPTION

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I. INTRODUCTION

In June 1960, the first combined oral contraceptive pill was approved for general use by the US Food and Drug Administration (FDA). Based on the results of relatively small clinical trials that had been conducted to assess their safety and efficacy, no evidence had appeared at the time of the FDA approval to suggest that oral contraceptives were associated with adverse or irreversible effects. Even in these early trials, it was recognized that the use of oral contraceptives was associated with side effects such as nausea, vomiting, and tender, enlarged breasts. But in the early 1960s, reports of serious complications resulting from the use of oral contraceptives began to appear in the medical literature. Jaundice, opthalmic abnormalities, myocardial infarction, thromboembolic phenomena, hypertension, and liver neoplasms have been among the reported serious and sometimes fatal complications associated with the use of oral contraceptives. Some of these complications are rare, however, and oral contraception continues to be considered a safe and effective method of contraception as attested by the large number of users--an estimated 50 million women worldwide, including about 10 million users in the United States.

In the following sections the risks and benefits of three modalities of hormonal contraception--postcoital contraception, injectables, and oral contraception--will be considered. Because other methods of hormonal contraception such as vaginal rings and implants are still experimental and are not yet available for general clinical use, they will not be reviewed.

II. POSTCOITAL CONTRACEPTION

The administration of large doses of estrogen appears to be effective in preventing pregnancy in cases where intercourse was unprotected. If it is to be effective, therapy should start within 48 hours of intercourse, and usually consists of a five-day regimen of 5 mg ethinyl estradiol, 50 mg diethylstilbestrol, or 30 mg of conjugated estrogen (Premarin) per day. Because the effect of the estrogen is postovulatory rather than postcoital, the estrogen is ineffective if administered before ovulation or after implantation. Once implantation has occurred, exogenous estrogens are ineffective in disrupting pregnancy (1).

The postcoital administration of large doses of estrogen is associated with high rates of side effects, primarily nausea and vomiting (Table I), which may be attenuated with antiemetics. The primary complication of postcoital estrogen therapy is continued pregnancy. The failure rate of estrogen therapy has not been adequately documented since in any study the number of women who were pregnant is unknown. In a review of postcoital contraceptives, Aref and Hafez (1) reported 29 pregnancies, 3 (10.3%) of which were ectopic, among 9000 women treated with postcoital estrogens. In view of the teratogenic and carcinogenic effects in the offspring (male or female) of women who took diethystilbestrol during pregnancy (3), therapeutic abortion should be considered for all women who continue to be pregnant after postcoital estrogen therapy.

A safe, effective, and practical alternative to postcoital estrogen therapy is the vacuum aspiration of the uterine contents in women whose

menstrual periods are delayed by no more than two weeks (4). This procedure (menstrual regulation) would decrease the proportions of patients who were not pregnant and who were subjected to an unnecessary procedure.

Progestogens have been evaluated as postcoital oral contraceptives when taken within one to three hours after coitus (5, 6). Drug regimens evaluated include 0.8 or 1.5 mg quingestanol acetate, and 0.4 or 0.35 mg d-norgestrel. The failure rate associated with this method of contraception is about 2 to 4 failures per 100 woman-years and appears to be only slightly higher than the failure rate associated with the daily administration of progestogen-only pills ("minipills").

III. LONG-ACTING PROGESTOGEN CONTRACEPTION

Since 1963, depot medroxyprogesterone acetate (DMPA), a synthetic progestogen, has been extensively evaluated in clinical trials as a long-acting contraceptive. Although other long-acting steroidal contraceptives such as 200 mg norethisterone oenanthate administered every 12 weeks or 2.0 mg quinestol combined with 2.5 mg quingestanol acetate administered every 28 days have been evaluated, DMPA is the only long-acting injectable preparation that has been extensively evaluated and is commercially available in a number of countries. Several DMPA regimens have been evaluated, including 150-250 mg administered every three months and 250-450 mg administered every six months. The most extensive experience has been accumulated with 150 mg DMPA given every three months (90 days).

Nash (7), in a recent comprehensive review, critically assessed the performance and safety of 150 mg DMPA administered every three months. The following remarks are principally based on data presented by Nash. DMPA

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(150 mg every three months) is an effective contraceptive. The pregnancy rate associated with DMPA ranged from 0 to 1.2 per hundred woman-years in 20 studies that included 36,817 women with 734,278 woman-months of use. The rate compares favorably with the failure rate of combined oral contraceptives and IUDs.

The critical issue with DMPA concerns its carcinogenic potential: breast and cervical lesions have been reported for women using DMPA. The concern over breast cancer arises from the finding that DMPA therapy causes an increase in the number of breast nodules, some of which metastesized, in beagle dogs. The incidence did not significantly increase until after three years of DMPA therapy (8). Table II summarizes the incidence of reported breast lesions from several large studies. None of the patients reported by Rall et al (9), 2 of the 7 reported by Schwallie and Assenzo (10), and 4 of 14 patients with breast lesions reported by Schwallie (11) had carcinoma.

Powell and Seymour (13) first reported an increased rate of abnormal cervical cytology (dysplasia and carcinoma in situ) among women using DMPA. The carcinoma in situ (CIS) rate was 9.8/1000 for DMPA users compared to 5.0/1000 for the general clinic population. Schwallie (11) reported a 3.0/1000 CIS rate for 3857 women; Hall et al. (9) reported no cases of dysplasia or CIS among 1382 DMPA users; and Dodds (14) reported a cervical dysplasia rate of 4.2/1000 among 1883 DMPA users. These rates do not appear to be higher than the prevalent rate of CIS in the United States, which is about 3 to 9 per 1000 women (15, 16).

The data on breast lesions and abnormal cervical cytology suggest that DMPA does not have a carcinogenic potential. However, before such an

assessment can be made, it will first be necessary to assess the incidence of these lesions in comparable populations not contracepting with DMPA.

The most common side effect of DMPA is menstrual irregularity. Nash (7), in a review of the literature on DMPA, reported that amenorrhea occurs in 20 to 40 percent of the patients in the first months of use and increases to about 60 to 70 percent of the patients by the second year of use. Among women who are not amenorrheic, unpredictable bleeding is characteristic during the initial months of therapy. Schwallie and Assenzo (10) reported that among women receiving 150 mg DMPA every 90 days, about 35 percent had 12 to 30 days of spotting, bleeding, or both per month at three months. This percentage decreased to less than 10 percent by the second year of use. While some investigators (see ref. 7) have found that estrogen supplementation (0.5 mg stilbestrol or 0.02-0.04 mg ethinyl estradiol) for 7 to 10 days each month is useful in regulating menstrual irregularities, other investigators have found estrogen supplementation to be less useful. Comparative double-blind trials will need to be conducted to assess the usefulness of estrogen supplementation.

Another concern with the use of DMPA has been the return to fertility among women who discontinue use. A uniform finding among investigators is that a delay occurs in the resumption of normal menstrual cycles. McDaniel and Pardthaisong (17) reported that among 135 women who discontinued DMPA use in order to become pregnant, 76.8 percent became pregnant within about 16 months of the last DMPA injection. Schwallie and Assenzo (10) reported that 82 percent of 115 women became pregnant within 15 months of the last DMPA injection. These cumulative pregnancy rates are lower than the pregnancy rates after discontinuation of IUDs (about 88% by 12 months) or oral

contraceptives (about 94% by 12 months). Further studies will be necessary to evaluate this apparent delay in fertility and its relationship to DMPA therapy. Because of the apparent longer delay in return to fertility after DMPA use, some physicians do not recommend DMPA for the nulliparous woman.

IV. ORAL CONTRACEPTIVES

Combined Oral Contraceptives

While many other controversies surround the use of oral contraceptives, their effectiveness has not been an issue. When assessing the effectiveness of oral contraceptives (OCs), a distinction must be made between their theoretical effectiveness (estimated to be about 99.9%) and their use-effectiveness which measures the protection against pregnancy under use conditions. The failure rate of OCs under use conditions has been estimated to be 0.5-5 pregnancies per 100 woman-years. The use-effectiveness of OCs depends primarily on whether the tablets are taken according to the prescribed regimen. Failure to adhere to the prescribed regimen will increase the probability of pregnancy, perhaps more so with those OCs containing reduced amounts of estrogen/progestogen.

Numerous adverse reactions have been observed in women using oral contraceptives (Table III). Among the serious and sometimes fatal adverse reactions which have been associated with OC use are thromboembolic disorders, myocardial infarction, and liver neoplasms. Other less serious reactions include nausea, vomiting, dizziness, headaches, breast changes, edema, and weight gain which have been usually attributed to an excess of estrogen; and depression, tiredness, and changes in appetite which have been attributed to a progestogen excess. While some of the side effects associated with OC use can be determined objectively, e.g., hypertension,

others are determined subjectively, e.g., changes in libido. No adequate method exists to evaluate whether these side effects result from OC use or whether they are simply an associated finding. The side effects associated with OC use are related to variables other than the amount and type of estrogen and progestogen used. Figure 1 shows the incidence of complaints among three ethnically different populations in which the same OC preparation was used. The differences in the proportions of women with complaints might be attributed to the ethnic, nutritional, and cultural differences in the three populations. However, large differences in the occurrence of some side effects have been observed in populations where ethnic and nutritional differences were not a factor (Figure 2).

To assess the incidence of side effects related to OC use, Goldzieher et al. (19) conducted a double-blind, placebo-controlled clinical trial using five different preparations in identical capsules. The trial included one "high" estrogen (0.1 mg ethinyl estradiol daily) sequential OC, one "high" estrogen (0.1 mg mestranol daily) combined OC, one "low" estrogen (0.05 mg mestranol daily) combined OC, one progestogen-only OC, and a placebo. It was found that the incidence of side effects in the pretreatment cycle could not be used as a baseline to measure the incidence of side effects, except for nausea and vomiting, after starting OC use. All side effects with the exception of nausea and vomiting declined from their pretreatment incidence for women who used the placebo preparation. A significant increase in nausea, vomiting, headache, and nervousness was demonstrated in the first pill cycle only with the high-estrogen agents. The frequency of all other symptoms for the contraceptive preparations was similar to that associated with use of the placebo.

The complications of oral contraception which are of greatest concern are its possible carcinogenicity and its association with hypertension and thromboembolic, liver, gallbladder, and heart disease.

Two large prospective studies are currently being conducted to assess the risks and benefits of oral contraception (20, 21). The Walnut Creek Contraceptive Drug Study (United States) was started in 1968 to determine the side effects of oral contraceptives by comparing the health status of users and nonusers. Over 18,000 women have been enrolled in this study. In the United Kingdom, the Royal College of General Practitioners in 1968 undertook a prospective study of 23,611 OC acceptors and 22,766 nonacceptors. Also in 1968, the Family Planning Association of England started a prospective study to provide an assessment of the benefits and risks of different methods of contraception. In this study, a total of 17,032 women are being followed up.

In addition to the above prospective studies, numerous other studies have evaluated the safety of oral contraception. Since the occurrence of some adverse reactions to oral contraception is rare, the epidemiologic case-control study has frequently been used to assess the increased risk of these reactions among OC users compared to nonusers. In these studies, OC use among women with the adverse reaction, e.g., thromboembolic disease, is compared to OC use among a control group of women who do not have the adverse reaction. At best, these studies can only establish an association and not a cause and effect relationship between OC use and the adverse reaction. The studies may be subject to considerable bias if the control group is not appropriately selected. A detailed discussion of the disadvantages and advantages of case-control studies has previously been given

by Feinstein (22) and Goldzieher and Dozier (23).

Carcinogenicity of OCs

Although several case-control studies (24, 25, 26) have found a relationship between the exposure to exogenous extrogens and endometrial carcinoma, two prospective studies conducted in England (21, 27) have found no evidence of any relationship between oral contraceptive use and malignant or benign neoplasms of the uterus. These studies have also shown no relationship between OCs and malignant or benign neoplasms of the ovary, cervix, vagina, or breast.

The Royal College Study (21) found a decreased incidence of benign neoplasms (fibro-adenosis) of the breast among OC users, which decreased with increasing OC use. The rate of benign neoplasms of the breast was 10.6 per 1000 woman-years for non-OC users compared to 9.5 per 1000 woman-years for OC users during the first year of OC use, and 5.3 per 1000 woman-years for the fifth and subsequent years of OC use.

Thromboembolic Disease

Although case-control and other studies have demonstrated a relationship between OC use and venous thrombosis, pulmonary embolism, and cerebrovascular accidents, prospective clinical trials have not always confirmed this association. A study conducted by the Royal Australian College of General Practitioners (28) found a lower incidence of thromboembolic disease among OC users than in nonusers. In 1961, a clinical trial was undertaken in Puerto Rico (29) in which 4933 women were randomly assigned to a vaginal contraceptive method and 4965 women were randomly assigned to a high-dose oral contraceptive (75 mcg mestranol and 5 mg norethynodrel). Eighty-seven percent of the subjects were followed up for

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over eight years. No statistically significant increase in the incidence of thromboembolic disease in subjects using the OC could be demonstrated. The incidence of thromboembolic disease among the OC users was 0.86 per 1000 woman-years compared to 0.58 per 1000 woman-years for the control group.

The two prospective studies being conducted in England (21, 27) have, on the other hand, reported a significant association between thromboembolic disease and OC use. Vessey et al. (27) reported significantly higher first event rates for cerebrovascular disease, venous thrombosis, and pulmonary embolism (Table IV). These events rates were standardized for age, parity, social class, and use of tobacco (smoking). The Royal College Study (21) reported no association between coronary artery disease and the use of oral contraceptives, but did report a significant association between cerebrovascular disease and venous thrombosis (Table V). The Royal College Study did not demonstrate any relationship between deep or superficial venous thrombosis and the use of oral contraceptives. The study did, however, note an increase incidence of venous thrombosis, particularly superficial thrombosis, among women using the higher estrogen content preparations.

Two case-control studies (31, 32) conducted in England and Wales have indicated that the risk of myocardial infarction is significantly increased among OC users compared to nonusers. The data from these case-control studies have been reanalyzed by Jain (33) and Ory (34), both of whom noted that cigarette smoking is the most important factor in increasing the likelihood of myocardial infarction. No evidence appears to suggest that oral contraceptives alone increase the risk of myocardial infarction in the ab-

sence of other risk factors. However, cigarette smoking is associated with an increased risk of myocardial infarction, a risk which further increases for women who smoke and use OCs. The synergistic effects of smoking and oral contraceptive use appear to be greater among women over 40 years of age. The estimated death rate from myocardial infarction attributable to OC use is shown in Table VI. Among OC users, the risk of death from myocardial infarction is 17 times higher among women with predisposing conditions compared to women without predisposing conditions, and is 3.4 times higher for women aged 40 to 44 compared to women aged 30 to 39. Predisposing conditions to myocardial infarction include smoking, obesity, hypertension, diabetes, and type II hyperlipidemia.

Gallbladder and Liver Disease

The Boston Collaborative Drug Surveillance Programme (35) and The Royal College Study (21) have both reported an increased risk of gallbladder disease (cholecystitis and cholelithiasis) among OC users. The case-controlled Boston Study showed the estimated increased incidence of gallbladder disease due to OC use to be 79 per 100,000 women per year. The Royal College Study reported an increased incidence of 68 per 100,000 per year. In the Royal College Study, the incidence of cholecystitis was not related to the duration of OC use. However, the incidence of gallstones (cholelithiasis) progressively increased, beginning after about two years of OC use, to about twice the rate for the nonusers of OCs at about four to five years of OC usage. However, the prospective study of Vessey et al. (27) did not find a significantly increased risk of gallbladder disease among OC users when compared to nonusers.

Since the first report in 1972 (36) of a benign liver tumor associated

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with the use of OCs, over 138 such tumors have been reported in the English literature. Prior to 1972, hepatic adenomas were considered to be extremely rare. Warvi (37), in a 1944 review of the world literature, found only 67 cases. Since 1972, a number of investigators have reported the association between hepatic adenomas and OC use (38, 39, 40, 41). Edmondson (41) has noted that there are at least two factors which may be determinants in the risk of hepatic adenomas: the prolonged use of OCs and the type of synthetic estrogen used in the OC. Several investigators (39, 40, 41) have observed that hepatic adenomas are most frequently diagnosed in women who have used OCs for prolonged periods of time, and a significantly higher proportion of the hepatic adenomas occurred in women who had used OCs containing mestranol. To explain why women using OCs containing mestranol are at increased risk of hepatic adenomas when compared to women using OCs containing ethinyl estradiol, one hypothesis (41) has emphasized that mestranol, which differs from ethinyl estradiol in that the hydroxyl group at C3 has been methylated, is first metabolized by the liver to ethinyl estradiol. The presumed increased risk associated with the use of mestranol arises from attempts of the liver to demethylate the mestranol. It is, however, important to note the hepatic adenomas also have been reported for women using progestogen-only OCs. The incidence of hepatic adenomas among OC users is unknown, but has been estimated to be less than 1 in 500,000.

Although the liver tumors which have been associated wth OC use may be benign, they are associated with considerable morbidity and mortality. These tumors are usually extremely vascular. Kent et al. (40), in a review of 78 liver tumors, reported that 25 percent of the cases presented with hepatic rupture and hemoperitoneum which led to subsequent death in nine

(11.5%) cases. In the presence of an unruptured benign liver tumor, there is some evidence to suggest that the tumors tend to regress and decrease in size after discontinuation of OC use.

Hypertension

Although OCs produce some alterations in the renin-angiotensin system, the relationship between these alterations and the development of hypertension remains controversial. In some women, OCs produce a slight elevation in blood pressure, and the incidence of hypertension appears to increase with increasing duration of OC use. Data from the Walnut Creek Study (20) indicate that OC users are 6.9 times more likely to develop hypertension (blood pressure >140/90) than nonusers. The corresponding rate reported in The Royal College Study (21) was 2.6. After cessation of OC use, blood pressures usually return to pre-OC use levels. Spellacy and Birk (42) have reported that, while some women develop hypertension while using OCs, other women with preexisting hypertension may experience a reduction in blood pressure while using OCs. The significance of OC-induced hypertension and its long-term adverse effects on health has not been delineated.

Progestogen-Only Oral Contraceptives

During the 1960s, the progestogen-only pills (minipills) were developed after researchers discovered that small daily doses of progestogens prevented pregnancy but not necessarily ovulation. It was also assumed that lower steroid doses would have less effect on the reproductive and metabolic systems. An added reason for the development and use of the minipill is its suitability for women who have diseases or conditions which may be aggravated by estrogen administration, such as a history of diabetes

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or gestational diabetes, preexisting hypertension, prior thromboembolic problems, or liver disease. Also, the minipill may be more appropriate for women using combined OCs who have estrogenic-related side effects such as nausea and vomiting. The primary side effects of the minipill are related to menstrual irregularities: breakthrough bleeding and irregular menstrual periods (43). These menstrual irregularities are the main reason for discontinuation of minipills.

The pregnancy rate asociated with the use of minipills appears to be higher than that of combined OCs; the reported rates vary from 0 to 3.6 pregnancies per 100 woman-years. Some reports have indicated that an increased risk of ectopic pregnancy exists among minipill users. The percentage of pregnancies that are ectopic is about 4.0, a rate which is comparable to the rate for IUD users (43). The rate of ectopic pregnancy in the general population is estimated to be about 0.5 percent.

Some studies have shown that the nutrient content of milk as well as the volume are lowered among women using combined oral contraceptives (44). Some reports (43) have stated that minipills usually do not affect the quantity or duration of lactation. However, some progestogens, e.g., those belonging to the 19-nortestosterone group, have mild estrogenic effects, while others, e.g., those belonging to the 17-α-hydroxyprogesterone group, have no estrogenic effects. Any minipill to be used by lactating women should, therefore, be carefully selected.

V. COMMENT

In this review, some of the risks and benefits of hormonal contraception have been discussed. The principal benefit of hormonal contra-

ception is that it provides a highly effective contraceptive method: when used according to prescription, the associated failure rate is probably less than 1 per 100 woman-years. Although this review has perhaps emphasized the risks associated with the use of hormonal contraceptives, particularly OCs, these risks must be put into the correct perspective. As previously stated, the complications of oral contraception which are of greatest concern are its possible carcinogenicity, hypertension, and thromboembolic, liver, gallbladder, and heart disease. The reports which have associated these complications with OC use are based primarily on studies conducted in the United Kingdom and the United States. The relevancy of the results of these studies to other parts of the world, especially to the developing nations, has not been established. For example, the risks of thromboembolic disease among OC users in the United Kingdom and the United States may cause concern. However, in some areas of the world, such as Asia, where thromboembolic disease is a rare event but the maternal death rate is several times higher, the increase in the number of fatalities from thromboembolic disease as a result of OC use is perhaps negligible in comparison to the lives saved through the use of a highly effective contraceptive. Documented differences in the metabolism of exogenous steroids among different ethnic groups (18) and differences in the health, nutritional status, and susceptibility to disease among different cultural and ethnic groups further complicates the evaluation of the relative risks and benefits of hormonal contraception. It is, therefore, important that judgments concerning the safety of the use of steroidal contraceptives be made on the basis of their relevant risks and be pertinent to the population in which they will be used.

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TABLE I

SIDE EFFECTS ASSOCIATED WITH LARGE ESTROGEN DOSES AFTER UNPROTECTED COITUS

Side Effect	Ethinyl-Estradiol 2–5mg Quotid x 5 Days *(N = 1418)* %	Diethylstibestrol 25–50mg Quotid x 5 Days *(N = 524)* %
Nausea	52.8	52.8
Vomiting	22.8	20.6
Breast tenderness	21.4	14.1
Menorrhagia	12.9	8.0
Abdominal pain	1.4	2.4
Headache	1.5	2.8
Other	8.5	7.2
None	31.6	34.5

Adapted from: Haspels, A A: Post-coital Oestrogen in large doses. IPPF Med Bul 6(2):3, 1972.

TABLE II

INCIDENCE OF BREAST LESIONS AMONG WOMEN USING DMPA

Reference	DMPA Regimen	No. Subjects	% With Breast Lesions
McDaniel and Pardthiasong (1973)	150mg/3 months Controls	1527 257	0.52 1.20
Schwallie and Assenzo (1973)	150mg/3 months	3857	0.18
Schwallie (1974)	Various regimens	11 500	0.12
Rall et al (1977)	150mg/3 months 450mg/6 months	19 875	0.00*

* *Rate of breast tumors only.*

TABLE III

ADVERSE REACTIONS OBSERVED IN WOMEN USING ORAL CONTRACEPTIVES

Serious Adverse Reactions	
•Thromboembolic disease	•Liver neoplasms
•Neuro-ocular lesions	•Cardiovascular disease
Known Reactions	
•Nausea	•Change in weight (increase or decrease)
•Vomiting	•Changes in cervical erosion and cervical secretions
•Gastrointestinal symptoms (i.e., abdominal cramps and bloating)	•Suppression of lactation when given immediately post-partum
•Breakthrough bleeding	•Cholestatic jaundice
•Spotting	•Migraine
•Change in menstrual flow	•Rash (allergic)
•Amenorrhea during and after treatment	•Rise in blood pressure in susceptible individuals
•Edema	•Mental depression
•Chloasma or melasma	
•Breast changes: tenderness, enlargement, secretion	
Possible Reactions	
•Anovulation post treatment	•Fatigue
•Premenstrual-like syndrome	•Backache
•Changes in libido	•Hirsutism
•Changes in appetite	•Loss of scalp hair
•Cystitis-like syndrome	•Erythema multiforme
•Headache	•Erythema nodosum
•Nervousness	•Hemorrhagic eruption
•Dizziness	•Itching

TABLE IV

STANDARDIZED FIRST EVENT RATES (PER 1000 WOMEN–YEARS) FOR CEREBROVASCULAR DISEASE AND VENOUS THROMBOEMBOLISM

	Method of Contraception		
	OCs	No OCs	$X^2_{(1)}$
Cerebrovascular disease	0.45	0.09	7.5*
Venous thrombosis and pulmonary embolism	1.06	0.33	10.5*

* $P < 0.05$.

Source: Vessey, M; Doll, R; Peto, R; Johnson, R; and Wiggins, P: A long-term follow-up study of women using different methods of contraception, an interim report. J Biosoc Sci 8(4):373, 1976.

TABLE V

STANDARDIZED EVENT RATES (PER 1000 WOMAN–YEARS) FOR CEREBROVASCULAR DISEASE AND VENOUS THROMBOSIS

	Method of Contraception	
	OCs	No OCs
Cerebrovascular disease	0.41	0.10
Venous thrombosis	3.16	1.05
Superficial thrombosis of leg	1.89	0.72
Deep thrombosis of leg	0.98	0.17
Other and unspecified sites	0.29	0.16

Sources: Oral Contraceptives and Health. An Interim Report From the Oral Contraceptive Study of the Royal College of General Practitioners. Sir Isaac Pitman & Sons Ltd., New York, 1974.

Kay, C R: Oral Contraceptives and Health: Thromboembolic Disease. Lancet 1:1381, 1975.

TABLE VI

ESTIMATED DEATH RATE (PER 100,000 WOMEN) FROM MYOCARDIAL INFARCTION ATTRIBUTABLE TO OC USAGE

	Age (years)	
	30–39	40–44
With predisposing conditions	25.7	86.2
Without predisposing conditions	1.5	5.1

Source: Ory, H W: Association Between Oral Contraceptives and Myocardial infarction. JAMA 237:2619, 1977.

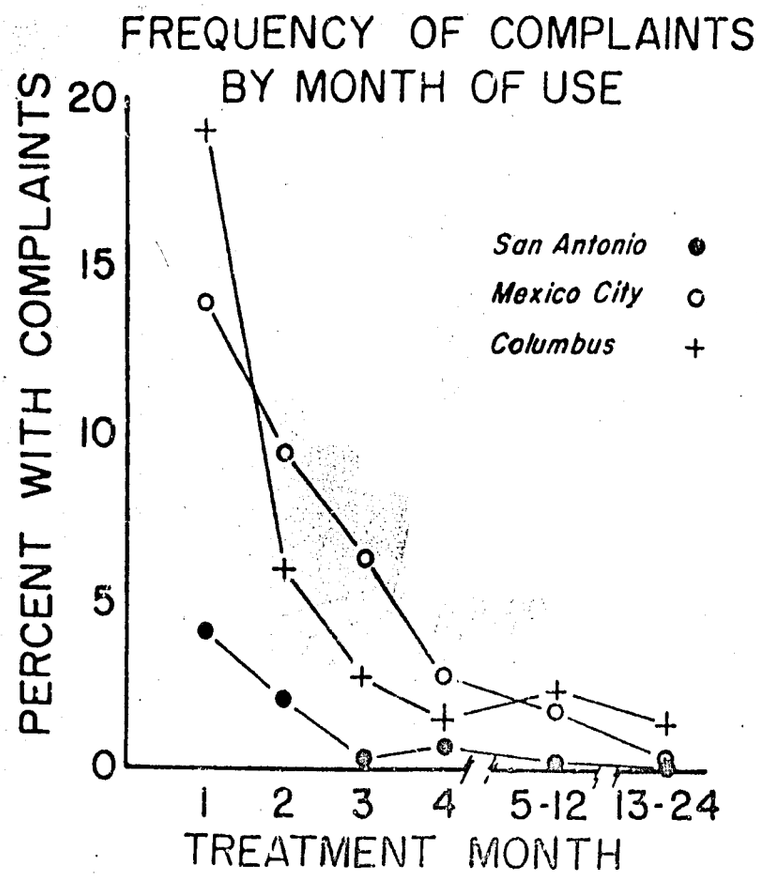

Figure 1. Symptom Frequency with the Same Oral Contraceptive, Tested in Three Ethnically Different Populations.

From: Goldzieher, J W: Perspectives in evaluating the safety and effectiveness of steroidal contraceptives in different parts of the world. Int J Gynaecol Obstet (in press).

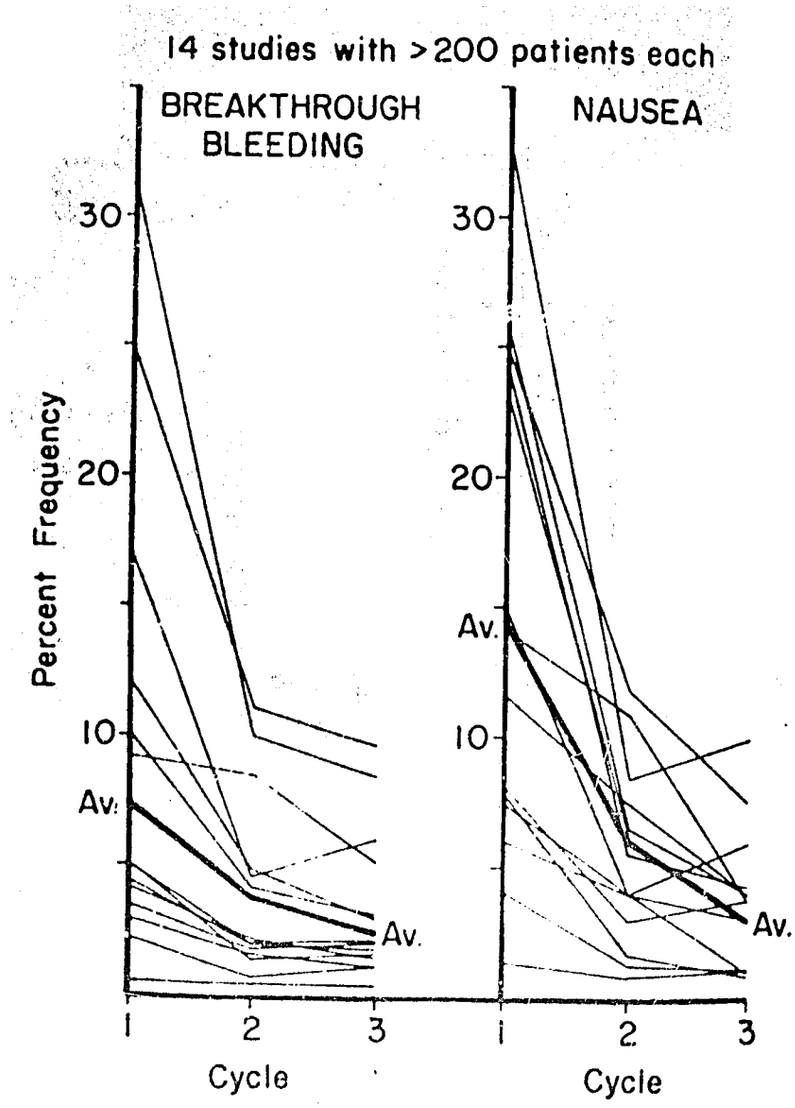

Figure 2. Symptom Frequency in a Clinical Trial Involving 14 U. S. Localities.

From: Goldzieher, J W: Perspectives in evaluating the safety and effectiveness of steroidal contraceptives in different parts of the world. Int J Gynaecol Obstet (in press).

A

EGYPT FERTILITY RESEARCH PROGRAM:

An Overview

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Presented at
Egypt Fertility Research Program Session
Egyptian Fertility Control Society
Fourth Annual Conference
Cairo, June 25, 1977

INTRODUCTION

The International Fertility Research Program (IFRP) was organized in 1971 with the objective of building research systems capable of accelerating the development, evaluation, and use of new fertility regulation technology. Through rapid analysis and timely reporting of data on the safety, effectiveness, and acceptability of new methods of fertility regulation at national, regional, and international meetings and conferences, the IFRP has spread awareness of available technologies and encouraged their early use in family planning programs and in general clinical practice. Central to the IFRP research system is the network of talented physicians and researchers, such as those in the Egypt Fertility Research Program (EFRP), that conduct clinical field trials. The objective of this presentation is to review the past, present, and future development of the Egypt Fertility Research Program as it relates to IFRP.

CONTRIBUTORS AND STUDIES

Two Egyptian physicians representing Cairo and Ain-Shams Universities were among the original 36 recruited internationally as contributors to the IFRP in 1971. Today there are 15 Egyptian contributors representing 12 clinics and hospitals including all five major universities (Table I). These contributors have submitted more than 28,000 forms and have conducted or are in the process of conducting 83 studies covering all areas of fertility regulation. Figure 1 and Tables II and III give information on forms flow and study areas by time period. As you can see, the flow of forms and the number of studies have been increasing steadily.

The first three studies, done in 1971, collected data on inevitable, incomplete, and septic abortions. These studies documented the pressures exerted on the gynecologic services and blood banks who had to cope with treating these patients. Recently studies comparing dilatation and curettage (D&C), dilatation and evacuation (D&E), menstrual regulation, the use of prostaglandin analogues, and newer equipment for these procedures, such as the Battelle Hand Pump, have been added.

A major effort has been directed toward IUD research. Plans for the first IUD studies were initiated in 1972. Currently, modified inert and medicated devices are being evaluated and compared. Some studies are also being done to quantify menstrual blood loss, study the retention mechanism of certain devices through hysterography, and evaluate the impact on IUD expulsion rates and morbidity of performing endometrial aspiration before IUD insertion.

The EFRP began studies on female sterilization in 1974, and the Egyptian Fertility Control Society established a female registry in 1975. Through these efforts Egyptian contributors began to realize the significance of surgical contraception in the armamentarium of family planning techniques. Female sterilization is being requested by increasingly larger numbers of Egyptian women. Physicians are trying to meet this demand by evaluating new equipment, recent modalities of tubal occlusion, and modifications of already established techniques. Approaches include laparoscopy, culdoscopy, vaculap and minilaparotomy utilizing electrocoagulation, tubal rings, and Pomeroy as means of tubal occlusion.

The research area most recently adopted by EFRP contributors is monitoring obstetrical care using the IFRP Maternity Record. Several major centers participated in the 1976 global pretest of the Maternity Record, and EFRP contributors look forward to recording data on 24,200 maternity cases in 1977.

Innovative approaches to the technology and delivery systems for systemic contraception are underway. At Ain-Shams, a male-female systemic contraception study will be initiated. A tricycle pill study, to be publicized during Ramadan, will be launched at Assiut and Mahalla El-Kobra. A new approach to distributing systemic contraception through the husband as the head of the household will be evaluated in two rural communities in both upper and lower Egypt.

Other studies to be initiated in 1977 include a study of immediate postpartum IUD insertion and a postpartum female sterilization program at Cairo University.

A detailed overview of each of these study areas will be provided by my distinguished colleagues in subsequent presentations at this special EFRP session today.

PUBLICATIONS AND CONTRIBUTOR FEEDBACK

Results of Egyptian studies have been disseminated through conference presentations and publications in scientific journals. A list of these articles is attached; other papers are in process. Reprints are available from the IFRP library and from individual contributors.

Currently, the IFRP is providing one contributor, an active EFRP member, with editorial assistance in preparing an Atlas based on his IUD hysterography studies.

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TRAINING

A formal training program in the clinical use of prostaglandins for pregnancy termination was supported by IFRP and conducted at the Department of Obstetrics and Gynecology at the University of North Carolina Medical School in Chapel Hill. One Egyptian physician completed this training in 1971.

In November 1976, a data collection coordinator was trained for 3 weeks at IFRP offices and spent an additional week touring pertinent centers in the USA. Plans are underway to train another data collection coordinator and another physician during 1977 in computer analysis of IUD data being collected at his center.

Also, the IFRP has appreciated the opportunity to host several of the EFRP contributors in Chapel Hill when they have attended various training programs in areas of fertility regulation in the USA.

REGIONALIZATION

A new phase in the growth of the EFRP Contributor Network has emerged. The EFRP is now being encouraged to develop national and regional study capabilities and local expertise in designing and analyzing studies following the IFRP model. Contributing centers are being asked to participate in designing studies that utilize IFRP protocols and data collection instruments, collecting and computer processing data, generating standard summary tables, and analyzing and presenting research results. IFRF will assist, train, and provide the back up necessary to enable the country program to accomplish the transfer of these activities.

It is hoped that this EFRP session will accelerate the development of a regional program in Egypt and will help establish a central unit which will be able to assume data collection, processing, and monitoring for studies in the Egyptian centers. The implementation of the regional program will involve monumental organization tasks, both financial and scientific. We hope that the Egyptian National Family Planning Program and other donor agencies will assist in this transition until EFRP is capable of handling all phases of the studies.

The first phase of regionalization is usually to select and train a data collection coordinator capable of assimilating all data scanning and monitoring tasks for data collected by researchers in Egypt. One person, from Al-Azhar University, has already been trained by the IFRP. The IFRP is planning to train another data coordinator for EFRP soon.

One active center at Cairo has already taken another positive step by electing to collect and store their own maternity record data on magnetic tape at the Cairo University Computer Center for subsequent editing, querying, and analysis at IFRP. Another center at Ain-Shams has already sent some test tapes to the IFRP to test the feasibility of transfer of data in this manner. The ultimate goal is to fully process and analyse all data in Egypt.

PROSPECTS OF EFRP

It is hoped that EFRP, within the Egyptian Fertility Control Society, will follow a pattern of phasing in the various elements required for full regionalization and institutionalization of research capability in all aspects of fertility regulation. Through EFRP, each governorate in the country should have a

good data collection system for reporting its hospital treated abortions, maternity record data, female sterilization cases, family planning records, and community-based distribution records. Use of the existing IFRP record forms relevant to these areas, as they exist or in simplified versions of these forms, or even in Arabic translations, will ensure comparable data and should be encouraged by the EFRP. The feedback of this information can be used as the basis of annual reports, to improve services, or introduce new programs needed in a particular area.

In conclusion, I want to thank my colleagues for giving me the opportunity to review the past and present status of EFRP. I am very optimistic and hopeful of its prospective accomplishment and its collaboration with other regional programs in neighboring Arab and Islamic countries.

TABLE I

PARTICIPATING UNIVERSITIES AND INSTITUTIONS BY YEAR, NUMBER OF CENTERS AND CONTRIBUTORS, EFRP, 1971–1977

Year	No. of Centers	No. of Contributors	University/Institution
1971–73	2	2	Cairo – one center Ain-Shams – one center
1974	6	7	Cairo – additional center Al-Azhar – one center Alexandria Boulak-El-Dakrour
1975	10	11	Ain-Shams – additional center Assiut Mahalla-El-Kobra
1976–77	12	15	Ain-Shams – additional center Al-Azhar – additional center

TABLE II

NUMBER OF STUDIES BY STUDY AREA AND YEAR, EFRP 1971–1977

Year	MR &PT	IUD	FS	Mat. Rec.	Total
1971	3	–	–	–	3
1972	4	1	–	–	5
1973	1	4	–	–	5
1974	2	4	7	–	13
1975	6	6	1	–	13
1976	4	6	4	5	19
May, 1977	5	14	1	1	21
Total	**25**	**35**	**13**	**6**	**79**

In addition, 4 systemic contraceptive studies are proposed for 1977.

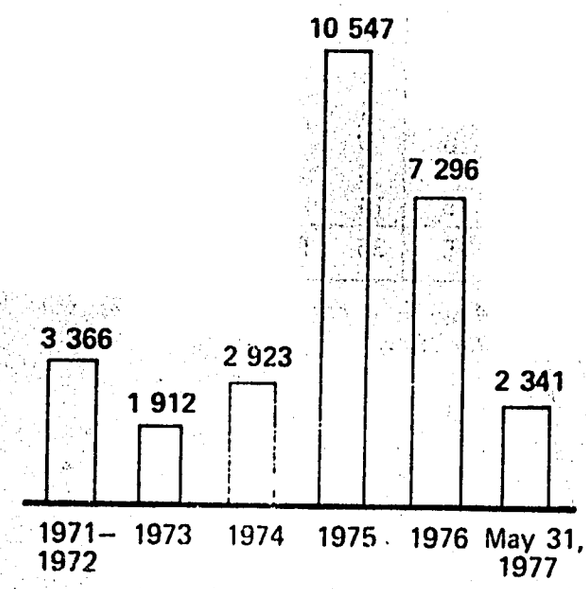
TABLE III

NUMBER OF FORMS BY STUDY AREA AND YEAR, EFRP

Year	MR &PT	IUD	FS	Mat. Rec.	Total
1971–72	3 366	-	--		3 366
1973	1 112	800	-		1 912
1974	750	1 949	226		2 925
1975	2 968	6 845	734		10 547
1976	705	4 775	832	984	7 296
May, 1977	161	1 502	365	313	2 341
Total	**9 062**	**15 871**	**2 157**	**1 297**	**28 387**

Figure 1

TOTAL NUMBER OF FORMS RECEIVED
BY TIME PERIOD
EFRP, 1971–1977



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1976–77	12	15	Ain-Shams – additional center Al Azhar – additional center

Publication List

1. Ragab, M I: Intrauterine devices (IUDs) on trial. Seventh World Congress on Fertility and Sterility, Tokyo and Kyoto, Japan, October 17-25, 1971.

2. Ragab, M I: A two-year trial of the heart and spring coil IUDs, 1972.

3. Ragab, M I: Jet ejector vacuum cannula for abortion: a new engineering principle. Contraception 5:199, 1972.

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B

RELATIVE RISKS OF VARIOUS MEANS OF FERTILITY CONTROL WHEN USED IN LESS DEVELOPED COUNTRIES

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I. INTRODUCTION

The aim of this initial review is to establish a sense of proportion, to ensure that a full range of questions is asked and to suggest some generalizations about family planning that can be considered in light of the remainder of this volume.

One important aspect of the scientific method is to recognize the limitations of available data. In the case of assessing the risks and benefits of fertility regulation they are considerable. However, unlike an astronomer who is exploring the universe in a purely intellectual way, as physicians and family planning administrators we are compelled to make decisions however weak the data. In the last analysis those decisions are judgments, not scientific conclusions.

II. THE VARIABLES

Method variables

All the most effective methods of fertility regulation involve certain dangers, but the problem of measuring risks varies. The side effects of using an IUD are largely dependent on the interval it is in use and any persistent infection it may have initiated. The risks of sterilization and abortion are mainly associated with conduct of the procedure and their assessment is relatively simple compared with the problem of handling the possible long-term side effects of systemically active contraceptives, where there is always the possibility of as yet unmeasured or unsuspected long-term effects. Additionally, the

systemically active methods can have positive therapeutic effects, which all considerations of family planning apart, may partially or totally outweigh any hazards.

When balancing the risks of a method against the risks of pregnancy and childbirth, assumptions must be made about contraceptive failure rates and about the use of alternative methods, but failure rates vary widely and are influenced by the stage in family building when a method is used.

Pregnancy variables

The developed world has enjoyed a remarkable decline in maternal mortality, even during the past decade, and some of the first published (1) comparisons of pill and pregnancy mortalities require revision. In 1972 the maternal mortality in England and Wales was 12 per 100,000 births, but in 1950 it was 70, and in 1940, 220. In 1890 the maternal mortality in England and Wales was 650. Unhappily, most of the developing world still suffers from high maternal mortalities. Tomkinson quotes a maternal mortality of 2000 per 100,000 live births in Ethiopia in 1973 and compares this with an estimate of 2500 for England in the time of Shakespeare (2).

Country variables

Most of our understanding of the side effects of fertility control options comes from studies in developed countries. In reviewing the implications of these studies for the developing world, one should take into account the following factors, in addition to variations in maternal mortality:

1. Are there any nutritional, ethnic or cultural differences in the reactions of various populations to the same method? For example, vegetarians on poor diets in India are very anemic, and the bleeding associated with IUD use is probably more troublesome there than in the West. Again the thromboembolic disease is rarer in the Orient than in the West. In a comparative study between Oxford and Bangkok, deep vein thrombosis was detected by fibrinogen labeled with radioiodine (^{125}I) infused with phlebography in 1.7 to 3.8% of postoperative hysterectomy and cancer surgery patients in Thailand and in 12 to 35% of cases in England (3).

2. Does endemic disease affect the method? For example, sickle cell anemia in West Africa or parasitic infestation of the liver in Egypt could alter pill side effects.

3. What personnel are available to supervise or perform the different techniques?

4. Is legal abortion available? This is a more important variable than may seem apparent at first. Early legal abortion is a very safe procedure. When available, its use must be realistically considered both alone and in conjunction with reversible methods.

Species variables

Finally, judgments on the risks of fertility regulation methods often rest in part on evidence from experimental animals. In most countries, animal tests are required before a product is licensed (4) and laboratory animal observations

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are the foundation of much biological research. Unfortunately, species differences are particularly marked in the case of reproduction, and no one animal provides an adequate model for the reproductive system of the human female.

III. FINDINGS

Our knowledge of the short- and long-term risks of various methods of fertility regulation is uneven and in some ways paradoxical. We know more about the dangers of a rare and difficult to study condition, such as thromboembolic disease among oral contraceptive users in the West, than we know about the likely death rate associated with female sterilization in a developing country. However, a number of generalizations can be made.

Generalizations

1. Condoms, spermicides and diaphragms are not associated with any risk to life, and morbidity is trivial. Condoms (and possibly spermicides) reduce the risk of venereal infections and may reduce the risk of carcinoma of the cervix.

2. The risks and benefits of steroidal pills, injectables and implants cannot be fully predicted in advance of use, but preliminary data is available on some aspects of the use of combined oral contraceptives. But even here a final measurement of the risks and benefits (including possible effects on the fetus) will only become available after even longer use.

3. Intrauterine devices increase the risk of pelvic infection. The risk of fatal illness is slight, except in the rare case when pregnancy supervenes, the device is not removed and infection occurs (5).

4. There is biological speculation that the use of periodic abstinence may be associated with a rise in the incidence of ectopic implantation and of fetal abnormality (6,7).

5. The risks of abortion, vasectomy and tubal ligation are almost entirely limited to the time of operation and a brief while afterwards. Legal abortion in the first 12 weeks of pregnancy has a mortality of less than 2 in 100,000, but abortion after 16 weeks is 20 to 50 times as dangerous as the operation before 8 weeks (8). Once over, abortion presents no long-term risk to life, and no serious long-term physical or emotional side effects are suspected, other than a possibility that certain methods may be associated with a rise in the prematurity rate in subsequent pregnancies (9).

6. Female sterilization has no serious long-term risk to life--although ectopic pregnancies have been reported in totally ligated women, these cases are exceptionally rare.

7. No long-term effects of vasectomy have been proved or are seriously suspected.

Risks and Benefits of Fertility Regulation in the Developing World

We have attempted to assess the risks and benefits of fertility regulation, with particular reference to developing countries, in two ways.

The Computer Model

Tietze, Bongaarts and Schearer (10) developed a computer model simulating reproductive events occurring during the child-bearing years of a hypothetical birth cohort of women using various regimens to control fertility. As these authors indicated, mortality is probably the best indicator of risk for a comparative evaluation of the consequences of either child-bearing or use of various methods of fertility control, although there are numerous other side effects, some potentially serious, related to use or non-use of means of fertility control.

Some of the information necessary to extend the Tietze model to less developed countries is weak, but there is enough to make some rough estimates and with these limitations in mind, we have rerun the model. Additionally, we have made some modifications relating to new information regarding the risk of use of oral contraceptives in developed countries among users who have predisposing conditions relating to fatal thromboembolic events compared to those without such conditions present. In using this model, we made no change in the original assumptions for successive age groups, mean fecundability, spontaneous fetal loss or percent of women who become permanently sterile. Some authors felt fecundability is lower in developed countries (11), based on nutritional factors, but other data do not bear this out (12). We have retained the mean duration of non-fecundability after a live birth at 4 months for developed countries; however, we have assumed this figure to be 12 months for less developed countries to allow for different patterns of breast-feeding.

Assumptions relating to contraceptive effectiveness are shown in Table I. For developed countries we have used data relating to use-effectiveness from the

original model (13) with the exception of the barrier methods, for which we have assumed a slightly improved use-effectiveness. The use-effectiveness of means used in less developed countries is assumed to be lower in categories for all means of fertility control, with the exception of intrauterine devices. Some studies from less developed countries report an appreciable failure rate with sterilization. Some studies of use-effectiveness of oral contraception in less-developed countries (LDC) (14,15) have shown rates comparable to those for the IUD. However, there is a considerable incidence of misuse of oral contraceptives reported in other studies. Accordingly, we have assumed a somewhat higher failure rate for this method in the LDC setting. Practically all studies relating to use of barrier methods show higher failure rates in developing country settings, and accordingly, we have estimated a higher failure rate for condoms and diaphragms (16,17).

Assumptions relating to mortality associated with pregnancy, childbirth, and the use of the various means of fertility control are shown in Table II. For developed countries, rates of maternal mortality associated with pregnancy and childbirth per 100,000 live births are shown, excluding deaths attributed to abortion, and are based on United States data from 1972-74. Since maternal mortality varies so widely in developing countries, two different levels have been used (18). That for a less developed country (Table II:LDCA) might be data representing a country which is fairly advanced on the pathway to development, (e.g. South Korea or Taiwan). Maternal mortality data shown under the column LDCB are based on data from the Matlab area of rural Bangladesh (19). Less than 10 percent of mortality in that study was attributed to induced abortion, and the figures presented are rounded off from that original data. Such mortality levels may be considered typical for rural areas largely unserved by health care

facilities in the poorest nations such as Bangladesh, Ethiopia, India, or Indonesia.

Figures used relating to abortion mortality are those presented by Tietze based on United States data from 1972-74. Mortality data for the two developing country settings were assumed to be twice (LDCA) and five times (LDCB) that in the United States.

The excess mortality resulting from thromboembolic events attributed to oral contraceptives is based largely on retrospective case control studies carried out in the United States and Great Britain (20-25). These rates are estimated by adding mortality from thromboembolic events other than myocardial infarction, i.e., pulmonary embolism and cerebral thrombosis, to mortality from myocardial infarction (See Apendices A & B). Strictly speaking, the addition of these two risk rates is not a legitimate procedure and is likely to exaggerate the risk. Mortality risks for myocardial infarction have been categorized by predisposing conditions such as hyperlipoproteinemia, hypertension, obesity, diabetes, and most importantly, smoking (22-25), and the data on other aspects of thromboembolic disease from Inman and Vessey have been recalculated by Jain for the presence or absence of predisposing conditions (20,22,23). Ory estimates that women who do not have these conditions predisposing to myocardial infarction make up about 70 percent of women of reproductive age in the United States (25), and the use of oral contraceptives by those women probably results in a relatively small increase in risk. However, oral contraceptives taken by women with predisposing conditions cause a considerable increase in risks. Epidemiologic studies of the occurrence of thromboembolic events among oral contraceptive users suggest that use of oral contraceptives acts as a kind of multiplier over the idiopathic occurrence of these events. Accordingly, we have arbitrarily

reduced the mortality risks relating to use of oral contraceptives in developing countries to take into account the believed lower risk of thromboembolic disease (3). It should also be noted that the proportion of women who have predisposing conditions present, particularly smoking and hyperlipoproteinemia, is also considerably lower in developing countries (26). One situation where a pill user in a developing country might be at greater risk than in a developed country would be in relation to the likelihood of receiving adequate treatment for a complication, e.g. gall bladder disease or myocardial infarction. Belsey has noted that risk of death from diseases uncommon in the United States and European countries, e.g. rheumatic heart disease or Chagas disease may be increased by use of oral contraceptives in developing countries.

Method-associated mortality related to use of intrauterine devices is based upon United States data with the assumption of twice the risk for LDCA countries and three times the risk for LDCB countries. These risks in developing countries may be somewhat underestimated in that a high hospitalization rate has been reported in the United States. Some of these hospitalizations might have had a fatal outcome in a developing country, where medical care facilities would not be as readily available.

Mortality relating to female sterilization is assumed to have declined somewhat in the United States, compared to the range of 10 to 20 per 100,000 estimated by Tietze. The extensive use of endoscopic procedures, particularly with application of tubal rings, appears to have reduced mortality in the United States (27). For LDCA and LDCB countries, two times and five times the United States risk is estimated (28). These risk levels are in keeping with a small series observed in developing countries by the International Fertility Research Program. The mortality data for female sterilization assume that interval

sterilization is done without pregnancy termination and by techniques other than hysterectomy. Although no deaths have been reported relating to vasectomy in most developing countries and in developed countries, there have been a few deaths caused by tetanus in some mass programs. Accordingly, a risk in LDCB of one death per million procedures is estimated.

Table III and Figures 1 through 3 display annual mortality rates per 100,000 non-sterile women for a variety of fertility regulation options. Had the data been based on all women in the simulated populations, it would have included some women or their partners who were sterile, but unaware of the fact because they were not currently trying to become pregnant. This alternative assumption would have reduced the conception rate, and therefore, the birth- and abortion-associated-deaths in the older age groups. In addition to presenting the annual number of deaths associated with the method and the conceptions that occur due to method failures, the findings have been presented as a percentage of the mortality calculated when no method of fertility regulation is adopted. (Table IV and Figure 4)

The model reveals the great increase in birth-associated deaths in developing countries, but other factors are also at work. Among women who do not use any means of fertility control the impact of the longer period of postpartum amenorrhea assumed in developing countries compared to less developed countries should be noted. Examination of data relating to use of abortion alone shows the large number of abortions required to control fertility, approximating twice to three times the number of live births. However, for all age groups in each of the country settings, the risk of mortality from relying on early abortion alone shows that this would be only one fourth to one twentieth as great as use of no means of fertility control.

In the populations using oral contraceptives, there are only a small number of birth-associated deaths. In all country settings and for all age ranges, use of oral contraception among women without conditions predisposing to thromboembolic disease shows a satisfactory mortality ratio with respect to use of other means of fertility control. The relative magnitude of the thrombotic risk, compared to other means of fertility control, is similar to the use of the other major means of fertility control without abortion, i.e., IUD and traditional methods.

The original model did not distinguish between women with and without predisposing factors. When women over 40 are considered as a single group, the relative risk of oral contraceptive use in a developed country is greater than with other methods. When women are divided into the two groups, then even those in the 30 to 39 age group with predisposing conditions in developed countries find themselves facing a risk which is higher than for other means of fertility control, although still about half of the risk of using no means of fertility control at all. As just noted, for those over 40 without predisposing factors the pill can remain a safe choice. (See Appendix A and B for assumptions regarding differential risks by predisposing factors.)

For women with predisposing factors, who are over the age of 35 in developed countries and over the age of 40 in the LDCA countries, the use of oral contraceptives becomes considerably more of a risk than use of no means of fertility control. In the poorest developing countries (the LDCB setting), use of oral contraception, even in the presence of predisposing factors, is still safer for women in this age group than use of no means of fertility control, and only about twice the risk of using traditional methods alone.

For IUD users, as for oral contraceptive users, most deaths are method-related and this remains a very safe technique in all country settings and for women of all ages. Use of the traditional methods (condom and diaphragm) results in a fairly constant mortality risk wholly related to birth-associated deaths. Use of traditional contraceptive methods backed up by abortion is by far the safest technique used in all country settings and by women of all ages. Although this regimen offers the safest choice of reversible contraception, mortality associated with tubectomy or vasectomy when "amortized" over 5, 10 or 15 years also places sterilization technology in the range of the very safest methods.

An Estimate Based on Program Data

The number of assumptions made in the model are sufficient to make it prudent to check the results using an alternative approach. In this second model, observation data from the 1974 National Acceptor Survey in the Philippines (29) are used as the basis for calculating method failures and method hazards. General assumptions have been made about fertility during the mean intervals of pregnancy protection observed in the program setting (Tables V through VII). No attempt has been made to assess risks by age groups or to distinguish between different LDC situations. The final estimates dealing with proven risks are of the same order as those for the computer model. Again the combination of early legal abortion with traditional or mechanical methods of contraception proves an order of magnitude safer than other reversible options (Table VIII).

IV. THE UNKNOWNS

Soon after the pill began to be widely used, a WHO committee commented, "The administration of biologically active substances to human beings must always be accompanied by some element of risk that cannot be avoided by the most careful and exhaustive scientific study of the drug before it is introduced (30)." Sir Alan Parkes encapsulated the major problem facing decision more directly. "It is always difficult to prove a negative and impossible to do so in advance. In fact we face the dilemma that no woman should be kept on the pill for twenty years until, in fact, a substantial number have been kept on the pill for twenty years (31)." We know today that we may even need to expand this cautionary statement to cover two generations--the user and her offspring.

We are forced to admit that we are still some way from being able to complete the final balance sheet for the risks and benefit of systemically active contraceptives. Indeed, a true analysis of what are potentially the most important long-term side effects still eludes us. Do oral contraceptives affect the incidence of one or more human malignancies? We will look at the evidence and the speculations surrounding the commonest cancer in the human female in the developed world.

Breast Cancer and the Pill

Whereas thromboembolic disease is a very rare entity with a death rate of a few in a 100,000, carcinoma of the breast and reproductive tract are fearfully common. Breast cancer alone kills 1 in 20 women by the age of 70 in developed countries (32). Many malignancies associated with the female reproductive tract are modified by circulating hormones and their incidence influenced by the

previous pregnancy history of the women. A few percent changes in the incidence of carcinoma of the breast would be much more significant in public health terms than the alteration in the incidence of thrombosis which has been demonstrated for women taking the pill.

Theoretically, the use of the pill could raise, lower or leave unchanged the incidence of cancer. It could act in different directions on different types and locations of cancer, and it could have a paradoxical effect at different stages in the development of the same malignant disease. The epidemiological problems posed by the study of the effect of the pill on cancer are formidable in the extreme. It is generally acknowledged that most malignant disease develops slowly over the course of years or decades. We should not overlook the fact that the literature on thrombosis and the pill is large, not because it is necessarily the most important side effect, but because in this case the action of steroids is immediate and, therefore, was detected relatively rapidly.

The development of the breast varies in different species (33). In some (e.g. kangaroo and dogs), the breasts develop at puberty and are capable of lactation independent of a preceding pregnancy. In a second group (e.g. rabbit, cat and rat) breast development and lactation is dependent on copulation and occurs in pseudopregnancy, even if fertilization does not take place. In most other mammals (e.g. sheep, cow, horse and subhuman primates), both breast development and lactation occur during pregnancy. The human female is unique in that breast development and lactation are separated. The former occurs at puberty (the human breast is exquisitely sensitive to estrogen) and physical development can be completed before any mature corpora lutea are formed and

progesterone secreted. But lactation only takes place as a result of pregnancy. This unusual pattern of breast development and physiology is probably related to an equally unique aspect of human sexual behavior--we are alone among mammals in that the breast has an erotic role for the woman's mate.

Therefore, no animal model is totally relevant to the problem of hormonal contraception and its possible effect on the human breast. Decisions based, for example, on the data from beagle dogs seem somewhat limited in their biological perspective.

How should we proceed? Fortunately, there is a considerable body of information relating to the epidemiology of human breast disease, some of which interlocks with broad principles discernable among other mammals. Beyond this point it is a case of reasoned guesses based on histological, statistical and pharmacological data and on general biological principles.

Breast cancer seems to be related to what Short called the "frustration of reproduction"(33). In the human situation there is a linear relationship between the age a woman has her first pregnancy and the probability of subsequently developing breast cancer--the earlier a woman has a pregnancy the less the chance of subsequent cancer (Figure 5) (34,35). The total number of pregnancies and whether breast feeding took place have been found not to be related to the risk of cancer. In the developing world, the incidence of breast cancer is still relatively uncommon when compared to that of the developed world.

While pregnancy early in life protects against breast cancer, a late first pregnancy (over age 35) raises the risk of disease even above that of the

nulliparous woman. The pattern extends to some other mammals. Breast cancer is common in nulliparous bitches (50 to 60% of unmated beagle bitches develop the disease), but it is rare after pups (33). If ovariectomy is performed before the first estrus, the chance of subsequent breast cancer is cut by 95 percent (36)

Ovariectomy also reduces breast cancer in cats (37) which, when it does occur, is disproportionately found in that rare animal, an intact queen that never became pregnant (38). Virtually all unmated rats develop breast disease, whereas only 4% of those caged with males suffer from the condition (39). In women, a second factor influencing breast cancer is the age at menarche (40), although the relationship is not as clear cut as in the case of the age of the first pregnancy. Menstrual exposure after the first pregnancy also appears to have some effect. Feinleib (1968) suggested that "the etiology of breast cancer is associated not so much with overproduction or underproduction of hormones of any specific type but with the cycle transitions of the breasts from hormone stimuli (41)". Short speculates that "the nulliparous breast may be stressed by a repeated succession of menstrual cycles, whereas following the first pregnancy there is a structural and functional transformation of the breast which protects it from further precancerous changes (33)". This speculation receives some support from the pattern of cancer in bitches where ovariectomy after the first estrus is associated with an 8 percent risk, but after two or more complete cycles, with a 26 percent risk of subsequent cancer (36).

These observations have important implications for those concerned with the risks and benefits of controlling human fertility. The postponement of the first pregnancy (by whatever means--abstinence, barrier methods, etc.), which is common in the contemporary developed world, and which the developing world is rightly seeking to emulate, has important short-term health benefits in relation

to maternal and infant mortality as well as the stability of marriage and social status of woman, but serious long-term risks. Not only is the postponement of the first pregnancy associated with a dramatic increase in breast cancer later in life, but the decline in the age at menarche which accompanies socio-economic development exacerbates this risk further.

We must recognize that the modern world subjects the human female reproductive system to some unusual strains. Women were adapted by evolution to a life where coitus began at, or soon after, puberty and continued until after the menopause, and where conception usually occurred after a small number of cycles of exposures. Most pregnancies went to term, and all babies were breast-fed for long intervals. In these circumstances a woman probably had no more than fifty ovulatory menstrual cycles in a life time, very few of which preceded the first pregnancy. Today, a woman may experience 300 or 350 cycles in a life time, and may easily have one hundred menstrual periods prior to her first child. No one would suggest that adolescent girls should deliberately have babies to protect their breasts in later life, but a reasonable long-term goal in medical research may be to develop pharmacological agents which not only give a woman the ability to control her own reproduction, but also ensure that she reaches the menopause unburdened by malignant disease. Can we imitate the hormonal changes of pregnancy without the necessity of a baby at the end of it?

The hormonal balance of a woman using the pill is more like that of pregnancy than regular menstruation, although the parallel is still a crude one. The duration of use of oral contraceptives and the scope of the studies so far completed does not allow a definitive judgment in relation to the pill and breast cancer but the observations on benign disease are interesting. The pill reduces a woman's chances of being admitted to the hospital with a lump in her

breast (42,43). Benign disease is generally considered to increase the risk of malignant changes later (44), and therefore, the initial epidemiological evidence on pill use is, at least, reassuring and, at most, actively encouraging. But, the complexity of the problem should not be underestimated and, of course, malignant disease itself is by no means a homogeneous condition.

There are still many unanswered questions concerning possible relationships between the pill and breast cancer, but it may help our thinking to recognize that the present, current way of using the female reproductive system is one of proven danger. The pill does at least take one step towards restoring the balance of hormone changes found throughout most of human evolution and, while it would be overoptimistic to suggest it necessarily represents a solution to the disease problems facing the modern woman, the preliminary evidence is that it may exert some benefit (45). If this benefit is confirmed it would be one of the major therapeutic breakthroughs of the twentieth century and one unrelated to the contraceptive value of exogenous hormones. In passing, we might note that this perspective suggests it may be wrong merely to continue to try and reduce hormonal dosage to the lowest possible amount, but rather we should be looking for a combination of hormones and a regimen which reproduce the effects of pregnancy on the young adult breast as accurately as possible.

Certainly, the Feminist on her platform who insists that the pill is "unnatural" is denying a million years of evolutionary history. Modern life is unnatural. The big step has already been taken. The pill may or may not represent an amelioration of an unnatural state of affairs, but it would seem that, if the human race survives, in a hundred or even a thousand years' time, we may still find that young women may benefit from some form of exogenous hormones reminiscent of pregnancy, whether or not they are needed to control fertility.

Some Things That Cannot Be Measured

Unlike other mammals, homo sapiens is sexually active during all seasons of the calendar, throughout all phases of the reproductive cycle, before, at and after ovulation, and during most of pregnancy and lactation. By any objective standard of comparative animal behavior the human mammal is obsessed with sex. In evolutionary terms coitus has become the prime social link between parents during the uniquely long childhood and adolescence which characterize our species. Sex, then, for us as social animals is associated with love and care of children, as well as with fertilization. The volitional control of fertility not only enhances the quality of human reproduction by helping to confine pregnancies to those years in a woman's life when they present least risk to her and maximum security for the offspring, but also adds greatly to the social aspects of sex. Any attempts to assign values to the risks and benefits of fertility control must include review of the problem at both these levels.

On the whole, analysts and decision makers have attempted to hide behind those variables open to measurement rather than face the broader issues (although usually it does not require a very profound insight into other people to realize that commonly they have been emphasizing certain aspects of the numerical data to fit their prior judgments on the wider issues). Most normal adults contemplating the use of contraceptives would almost certainly rate sexual activity as more important than other domestic leisure pursuits such as, for example, organized sport. Yet in Europe approximately 100 people a year die in sporting accidents in the Alps, although the total number of people engaged in Alpine pursuits is small compared with the number of Europeans engaging in pill-protected coitus. In the United States in one part of the Shenandoah River during a brief three-month period, there were 17 fatal canoeing accidents (46).

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Among men (aged 20 to 24) in the United States the death rate from drowning is 7.6 per 100,000 of the total population. It is even higher among adolescents (11.7 per 100,000) (47). And nearly all these deaths could be considered due to sport-related activities. There is approximately ten times the likelihood of death in the family if father buys an outboard motor than if mother takes the pill (48). Or to move to more exotic comparisons: The risk of death in one hour of flying a sailplane (4.4 per 100,000 hours), is greater than one year of pill use--and hang gliding (85 deaths up to 1975) is even more hazardous (49).

The statistics of the unusual are easy to pervert and perhaps the main justification for using them is not as an argument to convince someone that pills should be liberally available, but as a stimulus to trying to maintain a balanced view on contraceptive risks. Even clinicians seem to be easily unhinged when considering anything related to human sexuality. As recently as 1943, the famous British obstetrician Green Armytage wrote of diaphragms or condoms that the method (48):

> "...prevents, retards, or alters the normal degree of physiological absorption of human semen from the vagina, carries with it during the early months of marriage the risk of future sterility from failure of uterine development and endocrine asynchronization."

Another context for reviewing the epidemiology of contraceptive side-effects is to compare the political backlash created by the pill, which indisputably confers freedom of choice on a great many women, with other drugs and devices which have no therapeutic benefit, but where a vocal section of society strongly defends the personal right of people to hazard their lives. Among U.S.

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males as a whole (aged 15 to 64), there is a greater danger of dying in an accident associated with firearms (2.5 per 100,000 of the population) than there is of an oral contraceptive user dying of her medication. When the deliberate misuse of firearms and other acts of violence are considered the comparison is startling. A white woman in the United States has a greater chance of being murdered (2.3 homicides per 100,000 women all ages in 1970-71) than of dying from the pill. For a black woman, the risk of murder is 14.7 per 100,000; for a black male it is 77.2 per 100,000 and for a young black male (25 to 35 years old) 149.5 per 100,000. In other words, a young black male in the United States has a 100-times greater chance of being murdered than his wife or girlfriend has of dying if she chooses to use oral contraceptives. Yet little progress seems to have been made in legislation to control the use of firearms in the United States, although a great deal of political capital is made of the risks of oral contraceptives. In political terms, firearms which endanger the rest of society (and which psychologists sometimes remind us are phallic symbols) seem less threatened by the media and politicians than a medication which allows people to choose when to have their children and enhances one of the most important aspects of their individual private lives.

Cigarette smoking provides a second vivid perspective for reviewing pill hazards. In the United Kingdom there are approximately 30,000 deaths a year from lung cancer and an even greater number from cardio-vascular disease and bronchitis, which can also be linked to smoking. For every woman who dies as a result of oral contraceptives at least 1000 men and women die from the results of smoking. The annual mortality due to cigarette-induced lung cancer in Britain is 90 per 100,000 and for heavy smokers who retain the cigarette in the mouth between puffs, 410 per 100,000 (50). Using published data on the sales of oral

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contraceptives and of cigarettes (and assuming the carcinogenic effects of smoking are without any threshold and that there are no additional unpredictable mortalities due to the pill) then the use of oral contraceptives involves approximately the same risks as smoking one third of a cigarette every day.

For physicians yet another type of comparison may be useful. Most drugs have not been as closely monitored as oral contraceptives, but it is generally recognized that nearly all very widely prescribed medications carry a measurable risk to life. In Britain, doctors report an adverse reaction on a "yellow card" to the Committee on Safety of Medicines. Between 1964 and 1973, for a total of 17 analgesics and tranquilizers, there were 231 reported deaths. Phenylbutazone accounted for 141 of these deaths. Approximately three to four million prescriptions for the drug were written during this interval (51).

VI. WHO DECIDES

We have suggested that the issues relating to the use of contraception, abortion, and sterilization are wider than a mere balancing of the health risks of the method against the dangers of continued child-bearing. They involve judgments of aesthetics, human sexual joy, and relationships of the most profound and private sort between adults. The role of the medical profession and of drug regulatory agencies should be to provide the most up to date factual evidence available, in as objective a way as possible, being careful to point out those things which are still matters of speculation and attempting to use a terminology and a series of comparisons that are intelligible to the ordinary person. Beyond this, we suggest that ordinary persons should then decide for

themselves what they are going to do, just as they make a free choice about flying in aeroplanes, smoking cigarettes or skiing down snowy mountain slopes.

In the case of the surgical methods of fertility control, we suggest that similar considerations apply: we believe that those who provide the operations have an obligation to ensure that those seeking them are fully informed about the nature and consequences of sterilization and abortion; but beyond that point, the consumer must also be fully involved in the decision making.

In our opinion the political and media noise which surrounds FDA decisions in the United States of America is the result of a public asking questions which cannot be answered. It seeks a proof of safety when none can be given. And Americans, who are so ambivalent towards their medical profession, do not like to face the fact that doctors and scientists are not given supernatural powers of prediction, are yet, conversely, eager to sue them at the drop of a curette.

If we look objectively, at the history of the introduction and use of oral contraceptives, we will recognize that their widespread use is as much a response to the demand of individuals who made their private choices (admittedly often on an incomplete understanding of the evidence) and decided to use the method, as it is the end-point of a series of reasoned choices by medical scientists. Fortunately, the understanding which widespread use is producing tends to confirm the wisdom of these private choices. The same pressure for use has developed in relation to the use of medroxyprogesterone acetate (Depoprovera).

Medical Supervision

There are an estimated 2.5 million doctors in the world, of whom less than half a million practice among the three thousand million inhabitants of the

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third world. What is worse, probably only 50 to 60 thousand work as primary health physicians in rural areas (52). There are more Indian trained physicians in the National Health Service in Britain than in all the half million villages of India. Are the equations of risks and benefits for fertility control altered by possible patterns of supervision of a method?

We believe it is responsible to teach auxiliary workers to insert IUDs, and anyone who has performed early abortions and vasectomies usually concludes that these are also tasks which non-doctors (given appropriate supervision) can be trained to do. In at least two countries, auxiliaries are performing tubal ligation. We believe that with adequate training and sufficient practice, the risks associated with the various methods of fertility regulation we have reviewed will not be significantly raised if those procedures are carried out by non-doctors and may in some cases be less (because practice is probably a more important variable than breadth of background knowledge).

The case of oral contraceptive supervision raises some special problems. If we are honest, we must recognize that it is difficult to use a physiologically active compound "cautiously". The choice is often between widespread use or not using a method at all, and we may need to remind ourselves that any new systemically active method of contraception--whether a hormone-containing vaginal ring, a male pill or something to delay the menarche--will contain exactly the same logistical problems. Medical supervision *per se* will not protect against unpredictable risks. In the case of the pill, the ritual of medical supervision is all too often used in an unrealistic attempt to escape from this unpalatable fact.

In 1973 the IPPF Central Medical Committee reviewed the supervision and distribution of oral contraceptives (53). They accepted the demonstrable hazards of the method, but felt they were "difficult to predict by examination prior to use". They observed that:

> "the limitation of oral contraceptives distribution to doctor's prescription makes the method geographically, economically and sometimes culturally inaccessible to many women. As a consequence, deaths and sickness of women and children, which might otherwise be avoided by the voluntary limitation of fertility continue." The Committee then concluded "that whoever normally meets the health needs of the community, whether doctor, nurse, traditional midwife, pharmacist or storekeeper, can be an appropriate person to distribute oral contraceptives."

This landmark statement assisted the spread of community-based and household distribution systems of oral contraceptives in many countries, and these are proving very successful. But the IPPF statement is one about supervision, not freedom from side effects: it is a who-does-what statement, not a technical statement on the method. In the analyses performed above on the risks and benefits of the pill the only consistently important variables in both developed and developing countries, turn out to be the user's age and the presence or absence of associated risk factors, by far the most important of which is smoking. It does not require a medical qualification to elicit either of these factors. In 1974, one of the authors drafted a 'translation' of the IPPF Statement for the specific conditions obtaining in the United Kingdom. Twenty-four experts signed this letter to the British Medical Journal which in turn led to an invitation from the Secretary of State for Social Services to the Central

Health Services Council, the Medicines Commission and the Committee on the Safety of Medicine to set up a Joint Working Party on Oral Contraceptives. That Working Party took evidence from many sources and reported in 1976 (54). In its recommendations it stated "We do not regard it as necessary to restrict authority to issue prescriptions for oral contraceptives to doctors." It laid out simple guidelines for the use of oral contraceptives and concluded, "Nurses, midwives, health visitors and pharmacists have the relevant skills and knowledge which would enable them to be trained to fulfill the requirements," (the ability to take a simple history and some basic training in family planning). The Working Party even went so far as to add, "We would not, however, wish to restrict our recommendations to these persons."

A number of medico-political and even financially motivated objectors have been put against the British Working Party's report, but we suggest that the simplification of the pill distribution procedure, now occurring in both rich and poor countries, takes into account known facts about the hazards of pill use, and represents the best judgment of concerned people for both rich as well as poor countries.

VII. CONCLUSIONS

Where do we stand? We feel totally confident in the use of the barrier methods, first-trimester legal abortion and male and female sterilization. But it remains the obligation of those who provide these methods to make sure that those considering them are informed of their limitations and known side effects. The advantages of combining legal early abortion and the mechanical or traditional methods of contraception from the point of view of user risks, must be

noted. We observe that women of all cultures and religions seek abortion, but that ethical opinions are deeply divided and apparently irreconcilable. Perhaps nations should recognize this division and frame laws permitting a plurality of views.

The use of any physiologically active method of contraception introduces an element of the unpredictable. The pill has now been in use long enough to begin to ask numerous questions about some of the proven risks and benefits. The proven risks are considerably less than the risks of uncontrolled fertility and are of the same order of magnitude as the hazard of unplanned pregnancy when using less effective methods. This generalization applies to all women under 40 and to both developed as well as developing countries, although the ratio of benefit is greater in developing countries and greatest of all in the poorest countries where maternal mortality is highest. Among women over 40, those with predisposing factors to thromboembolic disease (of which smoking is the most important) are at a disadvantage if they use oral contraceptives compared with other methods. This disadvantage is marked in the case of developed nations and remains visible in the richer of the lesser developed nations, but high maternal mortalities overshadow the effect in the poorer countries of the third world, such as India.

We believe that physician prescription of the pill does little or nothing to reduce the main hazards and should not be a prerequisite of pill distribution in either rich or poor countries.

We believe that experience with the pill is now extensive enough to suggest that it is responsible to make it available to virtually any young person

requesting it, although we recognize that certain potential risks and benefits are still a matter for speculation. We know that the young adult female not using oral contraceptives, but postponing her first pregnancy by abstinence or a mechanical method of contraception, greatly increases her risk of developing breast cancer in later life. It may be biologically reasonable to suggest that an interval pill use will be no worse, and might in the long run be much better than this highly adverse consequence of the modern use of the female reproductive system.

The medical profession has set off on the road of using injectable contraceptives. We note there is a very strong demand for this method in many countries and predict an increasing use, although it will be some years before we know as much about the possible risks and benefits of this method as we do about those of combined oral contraceptives. There is no reason to assume that the risks and benefits should be the same, and many studies will need repeating.

We expect little important additional information from short-term epidemiological studies on oral contraceptive users, but think it is of the utmost importance to continue long-term surveillance, particularly in relation to all types of cancer and most especially of the breast and reproductive tract.

We take the evidence of adverse effects of the use of periodic abstinence seriously, but I do not think that data are sufficiently strong to condemn the method of those who wish to use it.

Like any physician faced with decisions over a patient, we can do no more than make sincere best judgments, and we have to be humble enough to admit that

even this short series of statements could contain within it an error of judgment, in which case literally millions of people may be seriously harmed. Unhappily, we have no more than a few facts and our own biological perspective as medical scientists to work with, and decisions do have to be made and will continue to be needed.

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TITLES AND LEGENDS

Tables I - VIII:		Titles on tables.
Figures 1		Annual Number of Deaths Associated With Fertility Control and Without Fertility Control per 100 000 Non-sterile Women by Age and Method of Contraception.
Figure 4:	**Title:**	Annual Number of Deaths Among Women Using Specified Methods of Fertility Control per 100 Deaths Among Women Using No Fertility Control Methods, by Regimen of Fertility Control, Age of Woman, and Country Setting.
	Legend:	None.
Figure 5:	**Title:**	Relative Risk of Developing Cancer of the Breast by Age at First Birth.
	Legend:	None.
Appendix A:		Title on appendix.
Appendix B:		Title on appendix.

Table I

ASSUMPTIONS OF METHOD FAILURE RATES (Q)
AND CONTRACEPTIVE EFFICACY (E) BY
METHOD IN DEVELOPED AND LESS DEVELOPED COUNTRIES

	Developed Countries		Less Developed Countries	
Method	Use-effectiveness (Q)	Contraceptive efficacy (E)	Use-effectiveness (Q)	Contraceptive efficacy (E)
Sterilization	0	1.0	.15	.9995
Oral Contraception	3	.99	4	.986
IUD	3	.99	3	.99
Condom & Diaphragm	15	.946	20	.926

Q=proportion contraceptors failing in one year
E=contraceptive efficacy--proportional reduction in monthly probability of contraception
F=Fecundity, monthly probability of conception in absence of contraceptive use, assumed to ≈0.25
$Q=1-(1-F[1-E])^{12}$, $E=1-\frac{1-\sqrt[12]{1-Q}}{F}$

Table II

ESTIMATED MORTALITY ASSOCIATED WITH MATERNITY AND USE OF FERTILITY CONTROL, BY AGE, METHOD, AND COUNTRY SETTING

Method and Country Setting	Age Group					
	15-19	20-24	25-29	30-34	35-39	40-44
Pregnancy and Childbirth (per 100,000 live births)						
Developed countries	11.1	10.0	12.5	24.9	44.0	71.4
Less developed countries-A	20.0	20.0	25.0	50.0	100.0	150.0
Less developed countries-B	700.0	400.0	500.0	500.0	500.0	800.0
Induced 1st Trimester Abortion (per 100,000 procedures)						
Developed countries	1.2	1.2	1.2	1.6	1.6	2.3
Less developed countries-A	2.4	2.4	2.4	3.2	3.2	4.6
Less developed countries-B	6.0	6.0	6.0	8.0	8.0	11.5
Oral Contraception Without Predisposing Conditions (per 100,000 users/year)						
Developed countries	1.2	1.2	1.2	1.9	4.0	7.3
Less developed countries-A&B	0.8	0.8	0.8	1.3	3.0	5.5
Oral Contraception With Predisposing Conditions (per 100,000 users/year)						
Developed countries	1.4	1.4	1.4	11.4	28.8	103.8
Less developed countries-A&B	1.0	1.0	1.0	6.0	13.0	63.0
Intrauterine Devices (per 100,000 users/year)						
Developed Countries	0.5	0.5	0.5	0.8	1.0	1.0
Less developed countries-A	1.0	1.0	1.0	1.5	2.0	2.0
Less developed countries-B	1.5	1.5	1.5	2.3	3.0	3.0
Female Sterilization (per 100,000 operations)						
Developed countries	10.0	10.0	10.0	10.0	15.0	20.0
Less developed countries-A	20.0	20.0	20.0	20.0	30.0	40.0
Less developed countries-B	50.0	50.0	50.0	50.0	75.0	100.0
Male Sterilization (per 100,000 operations)						
Developed countries	0	0	0	0	0	0
Less developed countries-A	0	0	0	0	0	0
Less developed countries-B	0.1	0.1	0.1	0.1	0.1	0.1

Table III

ANNUAL NUMBER OF LIVE BIRTHS, INDUCED ABORTIONS AND DEATHS ASSOCIATED WITH CONTROL OF FERTILITY, PER 100,000 NONSTERILE WOMEN, BY METHOD OF FERTILITY CONTROL, AGE, AND COUNTRY SETTING

Method and Outcome	Age group/Country type																	
	15-19			20-24			25-29			30-34			35-39			40-44		
	DC	LDCA	LDCB	DC	LDCA	LDCB	DC	LDCA	LDCB	DC	LDCA	LDCB	DC	LDCA	LDCB	DC	LDCA	LDCB
No control																		
Live births	50,770	41,440	41,440	61,400	45,940	45,950	59,290	43,170	43,170	39,930	35,930	47,700	34,210	34,210	34,210	31,680	23,940	23,940
Birth-associated deaths	5.6	8.3	290.0	6.1	9.2	183.8	7.4	10.8	215.9	13.8	20.[illegible]	199.7	21.0	34.2	171.0	22.6	35.9	191.5
Abortion																		
Induced abortion	99,502	99,502	99,502	133,664	133,664	133,664	132,041	132,041	132,041	127,278	127,278	127,278	106,209	106,209	106,209	64,779	64,778	64,778
Abortion-associated deaths	1.2	2.4	6.0	1.6	3.2	8.0	1.6	3.2	7.9	2.0	4.0	10.1	1.7	3.4	8.5	1.5	3.0	7.4
Oral contraceptives (without predisposing conditions)																		
Live births	1,150	1,590	1,590	1,940	2,650	2,650	1,910	2,600	2,600	1,770	2,410	2,410	1,350	1,840	1,840	650	890	890
Birth-associated deaths	0.1	0.3	11.1	0.2	0.5	10.6	0.2	0.7	13.0	0.4	1.2	12.0	0.6	1.8	9.2	0.5	1.3	7.1
Method-associated deaths	1.2	0.8	0.8	1.2	0.8	0.8	1.2	0.8	0.8	1.9	1.3	1.3	4.0	3.0	3.0	7.3	5.5	5.5
Total deaths	1.3	1.1	11.9	1.4	1.3	11.4	1.4	1.5	13.8	2.3	2.5	13.3	4.6	4.8	12.2	7.8	6.8	12.6
Oral contraceptives (with predisposing conditions)																		
Method-associated deaths	1.4	1.0	1.0	1.4	1.0	1.0	1.4	1.0	1.0	11.4	6.0	6.0	28.8	13.0	13.0	103.8	63.0	63.0
Total deaths	1.5	1.3	12.1	1.6	1.6	1.6	1.6	1.7	14.0	11.8	7.2	18.0	29.4	14.8	22.2	104.3	64.3	70.1
Intrauterine devices																		
Live births	1,150	1,140	1,140	1,940	1,920	1,920	1,910	1,890	1,890	1,770	1,750	1,750	1,350	1,330	1,330	650	640	640
Birth-associated deaths	0.1	0.2	8.0	0.2	0.4	7.7	0.2	0.5	9.5	0.4	0.9	8.7	0.6	1.3	6.6	0.5	1.0	5.1
Method-associated deaths	0.5	1.0	1.5	0.5	1.0	1.5	0.5	1.0	1.5	0.8	1.5	2.3	1.0	2.0	2.0	1.0	2.0	3.0
Total deaths	0.6	1.2	9.5	0.7	1.4	9.2	0.7	1.5	11.0	1.2	2.4	11.0	1.6	3.3	9.6	1.5	3.0	8.1
Traditional contraception																		
Live births	5,860	7,580	7,580	9,500	11,660	11,660	9,330	11,300	11,300	8,670	10,460	10,460	6,700	8,150	8,150	3,330	4,210	4,210
Birth-associated deaths	0.6	1.5	53.0	0.9	2.3	46.6	1.2	2.8	56.5	2.2	5.2	52.3	2.9	8.1	40.8	2.4	6.3	33.7
Traditional contraception and abortion																		
Induced abortions	7,564	10,273	10,273	11,444	15,483	15,483	11,332	15,317	15,317	10,9[illegible]	14,764	14,764	8,650	11,721	11,721	4,608	6,271	6,271
Abortion-associated deaths	0.1	0.2	0.6	0.1	0.4	0.9	0.1	0.4	0.9	0.[illegible]	0.5	1.2	0.1	0.4	0.9	0.1	0.[illegible]	0.7
Tubectomy																		
Live births	0	60	60	0	100	100	0	100	100	0	90	90	0	70	70	0	30	30
Birth-associated deaths	0	0	0.4	0	0	0.4	0	0	0.5	0	0	0.4	0	0	0.4	0	0	0.2
Method-associated deaths	10	20	50	10	20	50	10	20	50	10	20	50	15	30	75	20	40	100

Table IV

ANNUAL NUMBER OF DEATHS AMONG WOMEN USING SPECIFIED METHODS OF FERTILITY CONTROL PER 100 DEATHS AMONG WOMEN USING NO FERTILITY CONTROL METHOD, BY METHOD AND COUNTRY SETTING

Method/Country Setting	Age Groups 15-19	20-24	25-29	30-34	35-39	40-44
Developed Countries						
No method	100	100	100	100	100	100
Abortion only	21.4	26.2	21.6	14.5	8.1	6.6
Orals only without predisposing conditions	23.2	22.9	18.9	16.7	21.9	34.5
Orals only with predisposing conditions	26.8	26.2	21.6	85.5	140	462
IUD only	10.7	11.5	9.5	8.4	7.6	6.6
Traditional only	10.7	14.8	16.2	15.9	13.8	10.6
Traditonal and abortion	1.8	1.6	1.4	1.4	0.5	0.4
Less Developed Countries-Type A						
No method	100	100	100	100	100	100
Abortion only	28.9	34.8	29.6	20.0	9.9	8.4
Orals only without predisposing conditions	13.3	14.1	13.9	12.5	14.0	18.9
Orals only with predisposing conditions	15.7	16.3	15.7	36.0	43.3	179.1
IUD only	14.5	15.2	13.9	12.0	9.6	8.4
Traditional only	18.0	25.0	25.9	26.0	23.7	17.5
Traditional and abortion	2.4	4.3	3.7	2.5	1.2	0.8
Less Developed Countries-Type B						
No method	100	100	100	100	100	100
Abortion only	2.0	4.4	3.7	5.0	5.0	3.9
Orals only without predisposing conditions	4.1	6.2	6.4	6.7	7.1	6.6
Orals only with predisposing conditions	4.2	6.3	6.5	9.0	13.0	36.6
IUD only	3.3	5.0	5.1	5.5	5.6	4.3
Traditional only	18.3	25.4	26.1	26.2	23.8	17.6
Traditional and abortion	0.2	0.5	0.4	0.6	0.5	0.4

Table V

RISKS AND BENEFITS OF ORAL CONTRACEPTIVES IN MODEL DEVELOPING COUNTRY

Mean length of pill use in months	24
Cumulative pregnancy rate (24 months) per 100 in pill users	5
Assumed mortality due to pill per 100 000 users per year	2
Assumed maternal mortality per 1000 births	1
Assumed cumulative pregnancy rate (24 months) per 100 with no contraception	50
Risk of death per 100 000 pill users over 24 months (method = 4, pregnancies = 5)	9
Risk of death due to pregnancy among 100 000 non-users over 24 months	50
Advantage to pill users	5.5:1

Table VI

RISKS AND BENEFITS OF IUD USE IN MODEL DEVELOPING COUNTRY

Mean length of IUD use in months	44
Cumulative pregnancy rate (44 months) per 100 in IUD users	12
Assumed mortality due to IUDs per 100 000 users per year	1
Assumed maternal mortality per 1 000 births	1
Assumed cumulative pregnancy rate (44 months) per 100 with no contraception	90
Risk of death per 100 000 IUD users over 44 months (method = 3.9, pregnancies = 12)	15.9
Risk of death due to pregnancy among 100 000 non-users over 44 months	90
Advantage to IUD users	5.6:1

Table VII

RISKS AND BENEFITS OF CONDOM USE IN MODEL DEVELOPING COUNTRY

Mean length of condom use in months	12
Cumulative pregnancy rate (12 months) per 100 in condom users	12
Assumed maternal mortality per 1 000 births	1
Assumed cumulative pregnancy rate (12 months) per 100 with no contraception	30
Risk of death per 100 000 condom users over 12 months (method = 0, pregnancies = 12)	12
Risk of death due to pregnancy among 100 000 non-users over 12 months	30
Advantage to condom users	2.5:1

Table VIII

REVERSIBLE METHODS OF CONTRACEPTION AND LEGAL EARLY ABORTION

Method	Risks of Method and Pregnancy	Advantage to Users	Risks of Method and Legal Abortion	Advantage to Users
Pill	(4 + 5) = 9	5.5:1	(4 + 0.5) = 4.5	11:1
IUD	(3.9 + 12) = 15.9	5.6:1	(3.9 + 1) = 4.9	18:1
Condom	(0 + 12) = 12	2.5:1	(1) = 1	30:1

Assumed risk of legal early abortion is 10 deaths per 100 000 operations.

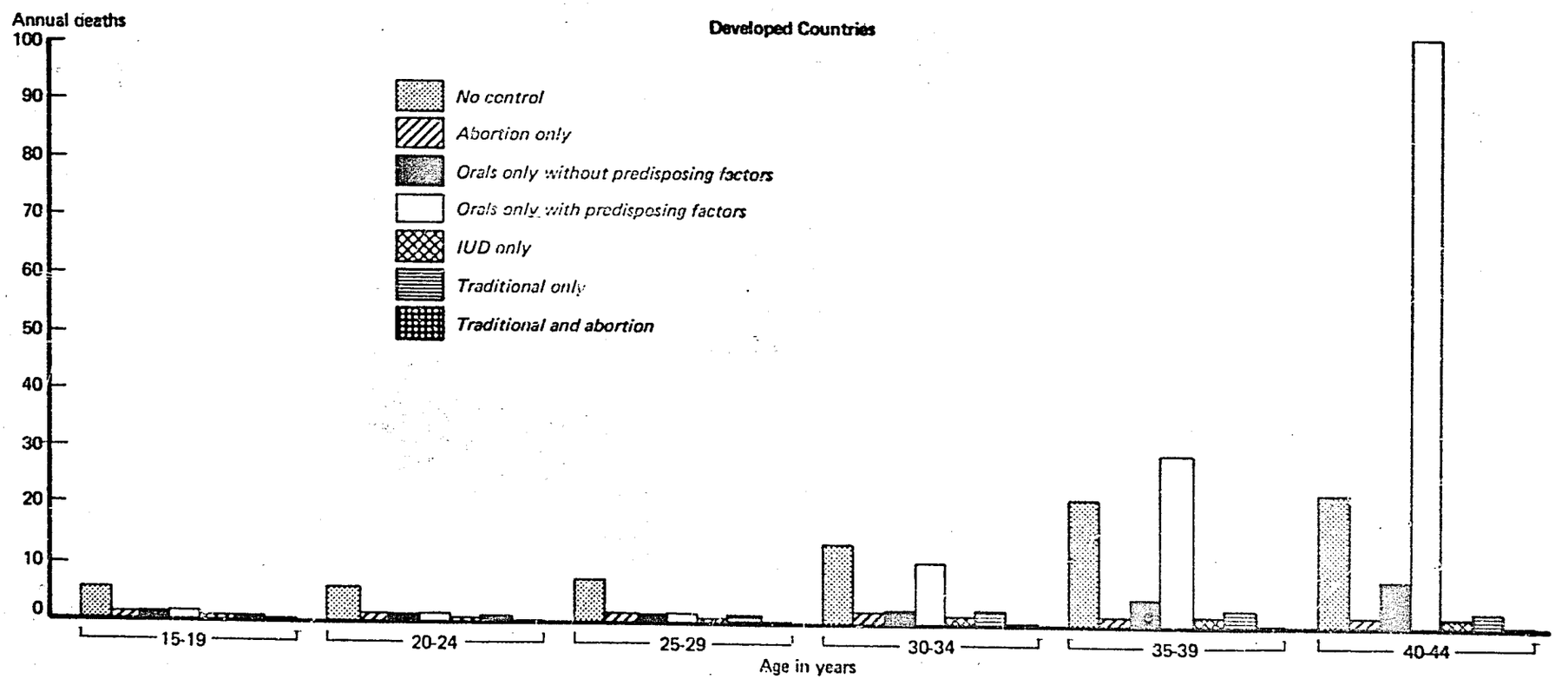

Figure 1. Annual Number of Deaths Associated With Fertility Control and Without Fertility Control per 100 000 Nonsterile Women by Age and Method of Contraception.

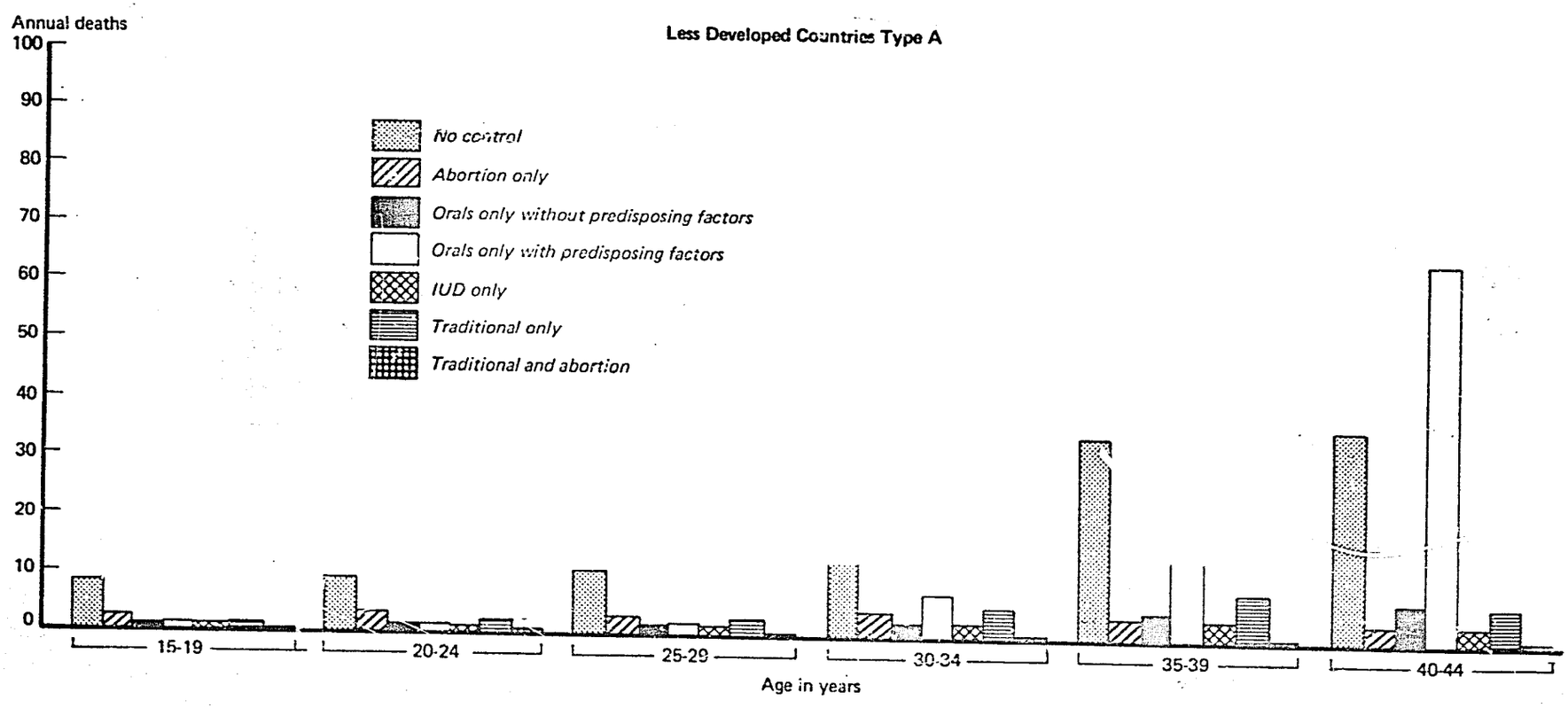

Figure 2. Annual Number of Deaths Associated With Fertility Control and Without Fertility Control per 100 000 Nonsterile Women by Age and Method of Contraception.

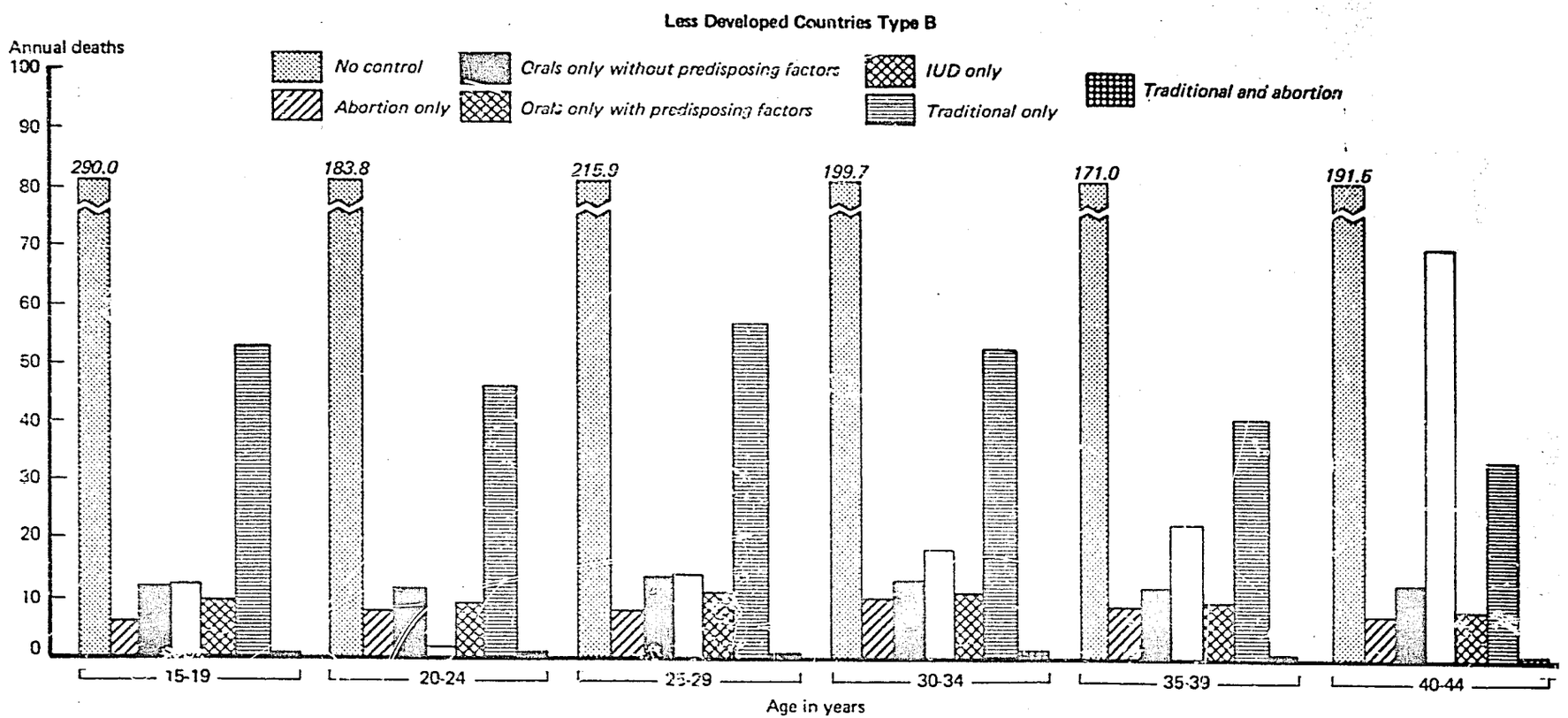

Figure 3. Annual Number of Deaths Associated With Fertility Control and Without Fertility Control per 100 000 Nonsterile Women by Age and Method of Contraception.

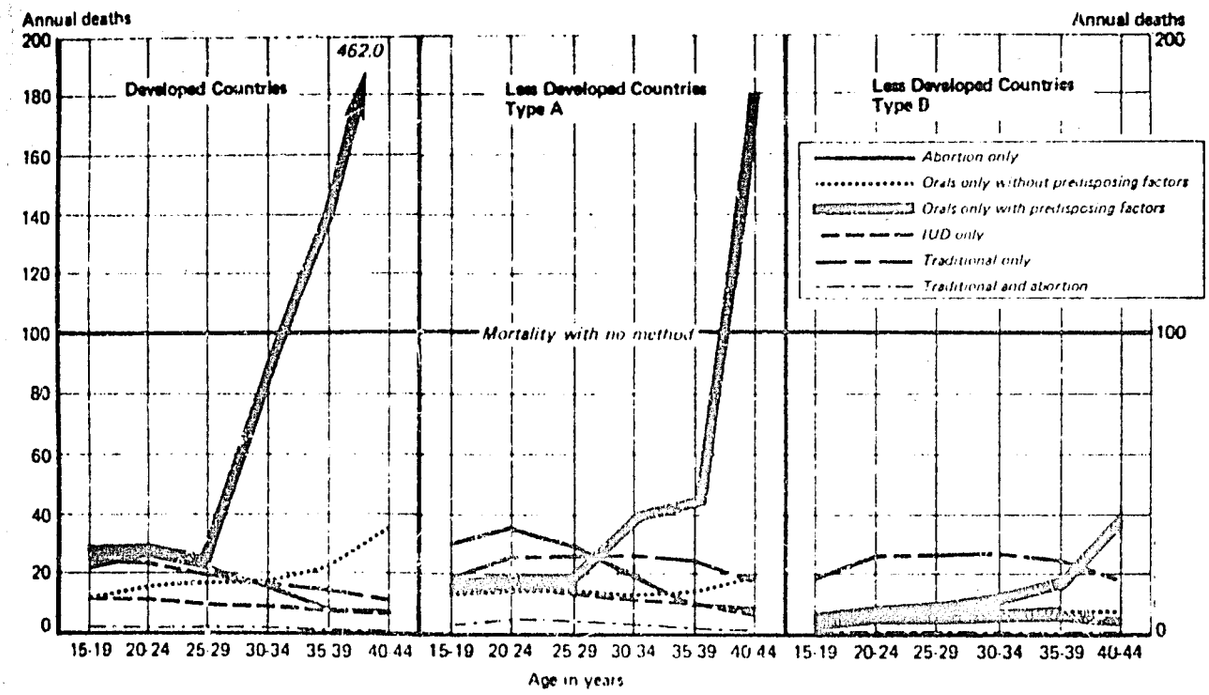

Figure 4. Annual Number of Deaths Among Women Using Specified Methods of Fertility Control per 100 Deaths Among Women Using No Fertility Control Methods, by Regimen of Fertility Control, Age of Woman, and Country Setting.

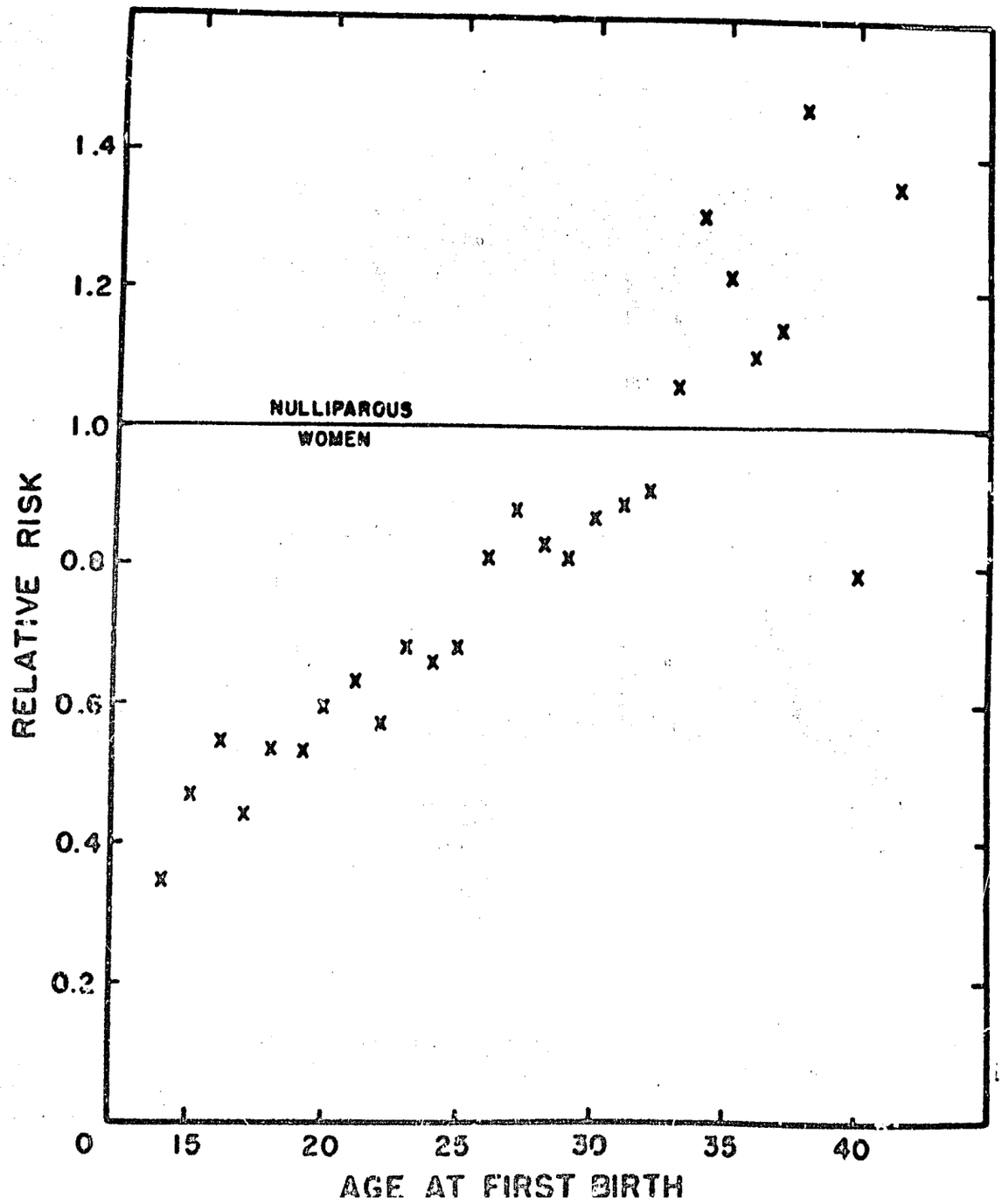

Figure 5. Relative Risk of Developing Cancer of the Breast by Age at First Birth. (MacMahon et al, 1970)

Appendix A

ESTIMATED EXCESS ANNUAL INCIDENCE OF FATAL MYOCARDIAL INFARCTION ATTRIBUTED TO ORAL CONTRACEPTIVES PER 100,000 USERS BY AGE AND PRESENCE OR ABSENCE OF PREDISPOSING FACTORS

Age and Author		Women Without Predisposing Conditions	Women With Predisposing Conditions
30-39	Jain (23)	0.6	9.0*
	Mann (24)	0.7	24
	Ory (25)	1.5	25.7
40-44	Jain (23)	3.3	54.6*
	Mann (24)	3.9	124
	Ory (25)	5.1	86.2

*Smoking only predisposing factor present

Appendix B

ASSUMPTION USED IN MODEL OF EXCESS ANNUAL INCIDENCES OF FATAL THROMBOEMBOLIC EVENTS ATTRIBUTED TO ORAL CONTRACEPTIVES PER 100,000 USERS, BY AGE AND PRESENCE OR ABSENCE OF PREDISPOSING CONDITIONS IN DEVELOPED COUNTRIES AND LESS DEVELOPED COUNTRIES

	Mortality from other than myocardial infarction with predisposing conditions				Mortality from myocardial infarction with predisposing conditions				Total mortality from thromboembolic events with predisposing conditions			
	Absent		Present		Absent		Present		Absent		Present	
Age Group	DC	LDC	DC	LDC	DC	LDC	DC	LDC	DC	LDC	DC	LDC
15-19	1.2	0.8	1.4	1.0	0	0	0	0	1.2	0.8	1.4	1.0
20-24	1.2	0.8	1.4	1.0	0	0	0	0	1.2	0.8	1.4	1.0
25-29	1.2	0.8	1.4	1.0	0	0	0	0	1.2	0.8	1.4	1.0
30-34	1.2	0.8	1.4	1.0	0.7	0.5	10.0	5.0	1.9	1.3	11.4	6.0
35-39	3.3	2.5	3.8	3.0	0.7	0.5	25.0	10.0	4.0	3.0	28.8	13.0
40-44	3.3	2.5	3.8	3.0	4.0	3.0	100.0	60.0	7.3	5.5	103.8	63.0

C

CURRENT ADVANCES IN FAMILY PLANNING TECHNOLOGY

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Fifth Expert Meeting on Comparative Fertility Research
Sterilization and Post Conceptive Regulation
IGCC Conference
Denpasar - Bali, January 15-18, 1977

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Advances in contraceptive technology sometimes assume quantum leaps. The introduction of drugs, such as the prostaglandins, and instruments, such as the laparoscope, bring a new dimension to the delivery of family planning services. Most developments occur, however, in a slow incremental fashion, permitting refinement of procedures so that they become safer to perform and more acceptable to the patient. Much has been learned in the past decade about family planning services, not only in the range to be offered and their method of delivery, but also in the accommodations required to meet the individual needs of communities.

In the field of systemic contraceptives, there is constant change in the formulation of various oral preparations. Today, we know that the patient's biologic response is different for estrogen pills of low and high potencies. These changes must be carefully measured and evaluated to find the appropriate preparation for a particular population. Because continuation rates of oral contraceptives are frequently disappointing, an assessment must be made of the symptoms and changes produced by the preparation which deterred the patient from using it. This can only be accomplished by reviewing a series of cases with a symptom grid and checking the effects produced by switching from various preparations. Once these subtle symptoms and their incidence are better understood, popularization of oral contraceptives can be enhanced.

The worldwide techniques of distribution of oral preparations and their presentation to prospective clients should be critically examined, and their packaging and marketing further explored. The International Fertility Research Program is currently investigating the acceptability of pills packaged under different brand names. The "Husband" brand is for use in societies where the

male is dominant; "Ramadan" is intended to appeal to the religious and cultural convictions of other communities.

Although preliminary studies carried out in the United Kingdom of bi-cycle and tri-cycle pill usage have been encouraging, they need to be undertaken throughout Southeast Asia as well. Transposition of Western results to deal with Eastern populations is not conducive to success in family planning programs.

Medication by injection is a very acceptable technique throughout the developing world, and this modality (Depo Provera*) might well become the basis for family planning services. We must review the varying dosage schedules which are available. Is there a significant difference between a 150 mg injection every three months and a 300 mg injection every six months? Early studies in Chile show that the latter schedule is quite acceptable, and serves to reduce the professional and patient time involved. Other methods of administering progestational agents are evolving. The Population Council is in the first phase of a study of a vaginal ring that will deposit a slowly released absorbable progestogen. Although this requires monthly removal and replacement, which is a deterrent to long-term acceptance, it nevertheless offers another approach to the provision of contraception predicated on hormonal control. Subcutaneous implants are also receiving renewed attention.

In the field of first trimester pregnancy termination, vacuum aspiration appears to be superior to Dilatation and Curettage (D&C). We must remember that the accomplished physician who has used curettage throughout his professional life might encounter difficulties with the initiation of vacuum aspiration.

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*Sterile Medroxyprogesterone Acetate

Knowledge and familiarity, not only of the equipment but of the technique, are critical as we develop new methods. In the field of second trimester pregnancy termination, much work remains to be done. The new analogs of prostaglandins and the new delivery systems, such as vaginal suppositories and intradermal and intramuscular injections, must be evaluated. The many side effects associated with prostaglandins have seriously impeded their acceptance. Other intraamniotic agents that minimize the complications produced by hypertonic saline are worthy of exploration. Encouraging results with the use of urea in combination with small increments of prostaglandin are appearing from Johns Hopkins University, and in England.

The gray zone of pregnancy termination from 12 to 16 weeks needs to be clarified. The combination of vacuum aspiration with curettage, using specially designed dilators and forceps, has proven to be most successful. Much of this effort was pioneered by the British, and good results have been reported. Not only should this technique be mastered, implemented, and evaluated, but it should also be compared to the use of intraamniotic agents, such as prostaglandin, saline, or urea. Perhaps most important is the study of the pregnancy that follows such a procedure. We must determine the effects of maximal cervical dilatation upon prematurity rates.

Other areas of fertility research in the field of pregnancy termination are the development of improved techniques of cervical dilatation. Early studies by Hulka have shown that once dilatation of 8 mm or more is necessary, increased force is required. Standard cervical dilators have been available for years, but there is room for exploration of newly designed instruments to minimize perforations and accommodate to the contour of the cervix. Hygroscopic methods also must be explored. The laminaria tent is well known, but today there are

polymers in which the volume of fluid absorbed and the period during which the dilator expands can be controlled.

The long-term effects of cervical dilatation on future childbearing are of the greatest importance. Clinicians should bear in mind that every time they perform a mid-trimester abortion, they must make every effort to minimize cervical trauma.

In the field of cannula design, there is general consensus that either a double- whistle cut (Karman) or a single-scoop aperture can work effectively. For more advanced gestations, it appears that the single-scoop cut offers more effective aspiration of larger fragments of tissue. Data from the IFRP, however, show that, regardless of the instrument design, the most important factor is the physician using it.

Intrauterine contraception remains an enormously challenging area of research. IUDs are among the most cost-effective methods in all family planning programs and yet, other than in sporadic cases, they have not achieved the expected level of acceptance. IFRP is actively involved in IUD research, and some of the major areas we are looking at include intrauterine metrology. It is critical to know the exact dimensions of the uterus if we are to properly fit an IUD. The work of Kamal and Zipper has shown that two basic configurations of the uterus exist; it may be conical in outline or triangular with a much broader fundus. These studies have also revealed that the location of the IUD within the fundal cavity is related to particular events. One recent critical study by Hasson, et al., shows that the number of major events is reduced when the IUD is slightly shorter than the internal-os-to-fundal measurement. This study must be replicated and expanded.

The IFRP is continuously involved in monitoring new IUDs as they appear. Among the devices now under surveillance are the Copper Loop, the Multiload device, the Soonawala Copper Y, and the postpartum Copper T. Some of the early studies on the pleated membrane have shown its small size to be advantageous, and it is currently being tested by Astawa in Bali. One of the modifications formerly considered promising was hydron-coating of IUDs. However, this process produces a stiffness that attracts calcification and deposits, making the device extremely rigid, and thereby generating an unacceptable level of bleeding events.

The IFRP has undertaken a project to increase patient acceptance of new IUDs and to make them more available. Despite the variety of devices, when compared to the Lippes Loop, it becomes apparent that the Loop has held up extremely well and can be considered the benchmark of IUD performance. As we look at the services women receive throughout the developing world, we see that the major events involving them with physicians or paramedics are the birth of a child or a pregnancy termination. This is the time when such patients are "captive" and highly motivated to receive a form of intrauterine contraception. For that reason, the IFRP, focusing on the Loop, has developed a number of modifications to make it acceptable for immediate postpartum or postabortion insertion. Among these adaptations are transverse arm extensions to fit that dimension of the immediate postpartum uterus. These extensions are biodegradable and can be made either of collagen or of polylactic acid over a gelatin core. They are designed to biodegrade from the ends inward so that at six weeks of uterine involution only a standard Loop D remains in the uterus. Anterior-posterior extensions are also under evaluation. Apelo has concluded a preliminary study of a modified Loop with a silastic sleeve on the upper arm that

has three anterior-posterior extensions. These are quite soft and yet allow sufficient fixation into the wall for retention in the immediate postpartum period. The 1-month expulsion rate for these devices was 2.0%.

The two other major concerns for IUD acceptance are pain and bleeding. We are exploring the addition of medicaments, primarily anti-bleeding agents, which can be added to an IUD. We have modified the Lippes Loop so that its transverse limbs are reduced to carry sleeves which will elute compounds to reduce the amount of bleeding. The modification under consideration at this time is a Lippes Loop carrying a tranexamic sleeve (AMCA) and is being studied in Cairo by Hefnawi. Promising developments that deserve exploration are the addition of Trasylol and other proteinase inhibitors for their ability to reduce the amount of bleeding associated with IUDs, and loading an IUD with an antiseptic that could be released over a period of a few days to prevent the development of pelvic infection, making the insertion procedure safer. The IFRP is also evaluating photo-reduced Loops and we now have one which has been reduced by 8.0 percent. It is hoped that the smaller configuration of the most acceptable shape (Loop D) will reduce the incidence of bleeding events. Another exciting modification is tapering of the Loop so that its upper limb is the thickest, and each limb, as one approaches the os, becomes slightly diminished in width. This device is expected to more suitably fit the contour of the uterus, and possibly reduce bleeding rates.

In the field of male sterilization we are dealing with a simple procedure which is almost entirely fool-proof; however, attempts must be made to shorten the period in which sperm persist in the semen. Flushing of the vas needs evaluation in a carefully controlled study environment with a cooperative

group of patients. There are early encouraging results with the use of nitrofurazone. This technique may facilitate elimination of the 12-week wait or the six to eight ejaculations that are required to produce aspermia. Another approach under assessment is the use of a bipolar cautery needle, the VASEAL, for sealing off the vas.

A preliminary report by Van Aasche from Leuven has demonstrated that the silastic Falope ring can be applied to the vas. Although his series is limited, it appears encouraging. If an occlusive method could be developed for the vas, then perhaps we could minimize the incidence of spermgranuloma and sperm antibody formation.

In the field of female sterilization, there is no doubt that minilaparotomy has become the procedure of choice throughout the world. Its simplicity, high acceptability rate in developing countries, and excellent results have focused attention on this method. The major contribution of Vitoon Osathanondh of Thailand has been to bring minilaparotomy to the attention of clinicians and investigators throught the world. Minilap can be further enhanced by occlusive devices like clips or rings that can be applied in the pelvis. This procedure should minimize patient discomfort and perhaps further reduce the small number of infections that can be attributed to lifting the tube outside the peritoneal cavity. Occlusive devices also offer an advantage in that they can be applied to the isthmic portion of the tube, thus avoiding either excision or ablation of the ampullary-isthmic junction or excision of a major portion of the tubal ampulla.

The increasing concern with the problem of reversibility must be applied to any method of sterilization. There is no doubt that isthmic anastomosis is the most successful form of reestablishing fertility in the female with a previously interrupted oviduct. Thus, a technique that can be restricted to the isthmic portion of the tube is essential.

Numerous adjunctive instruments have been developed at IFRP for further simplifying and facilitating minilaparotomy. A self-retaining retractor has been designed. Its small size will accommodate an incision not exceeding 2.5 cm, while a larger size may be used for the more obese patient with a deeper subcutaneous fat layer who requires a slightly larger incision. The original Vitoon tubal hook has also been modified by angling the handle in a backward fashion and introducing a slight curve to the elevating portion of the instrument.

The elevator dilators developed at IFRP should be compared to the standard Vitoon elevator. These devices are quite inexpensive, being made of a molded plastic that can be sterilized by any available solution or means, and can also be used for dilatation of the cervix. They possess a transverse barstop to minimize perforation and have a cervical curve which is identical to the Pratt dilator.

The need for investigation of long-term follow-up in the field of female sterilization is patent. International reports reveal that a significant incidence of delayed pregnancies occur beyond 12 months, and the etiology of these tubal failures and their frequency in relation to the various methods must be determined. Hasson's open laparoscopy technique, which eliminates the use

of a trocar and combines some of the advantages of minilaparotomy, appears to be easy to master.

The rate of dissemination of laparoscopic procedures throughout the world is related to the technical problems associated with the equipment and the establishment of adequate criteria for training personnel. New instrumental technologies ought to be developed rapidly to minimize the excessive costs and problems of the standard laparoscopic approach. We must develop a "stripped down" laparoscope that employs air sufflation, as opposed to either nitrous oxide or carbon dioxide. New procedures utilizing the laparoscope are under consideration, and although none are immediately ready for investigation, people involved in the field of sterilization ought to be aware of these activities.

The miniaturized laparoscopes which looked so promising a year ago are still with us, but have yet to be incorporated into serviceable models. The 4 mm operating laparoscope developed by Olympus appears to have adequate optics, for both diagnosis and surgery. As yet we have not determined what can be applied through the 2mm operating channel.

An operating laparoscope with an external diameter no greater than 7mm should be designed, because in many parts of the world this appears to be the critical number at which women will accept the procedure as a "large needle puncture."

In many developing nations there is considerable interest in establishing centers for microsurgical repair for women who desire reversal of sterilization. These techniques require exquisite training and specialized equipment. We must

rely heavily on the accomplishments of Winston, in particular, in instrumentation, suture needs, and the critical optics for these operations if we are to run successful programs. Initial careful selection of the patient(s) to be sterilized is crucial to avoidance of future demand for reversal.

The IFRP is involved in programs other than basic research. The organization conducts service-oriented programs for the introduction of technologies and their dissemination. It responds to requests for training sessions, primarily in minilaparotomy, from a government or any national fertility program. We strongly feel that local physicians should be part of such training programs and that model training units be developed within countries for this purpose. The IFRP is committed to transferring its programs abroad and to offering any country assistance in the evaluation of their family planning service.

I believe it is fitting to make an observation regarding the nature of research performed by the IFRP. The applied research in which the organization is involved is an outgrowth of the laboratory, bio-engineering, and requests from the field. Innovative ideas originated by local physicians must be pursued. We need their perspective and their contributions to conduct national programs, and the opinion of their patients regarding their particular family planning needs. Although we emphasize quality collection of data and rapid analysis via the computer, with its prompt feedback to the investigator, these are merely tools and do not represent research. They are only the instruments by which we can accomplish a rapid evaluation of the efforts in applied clinical research.

D

METHODOLOGY
SERIES NO. 23

INTERNATIONAL FERTILITY RESEARCH PROGRAM
CONFERENCE PAPER

SOME REPRODUCTIVE PARAMETERS IN HUMAN FERTILITY

By
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SOME REPRODUCTIVE PARAMETERS IN HUMAN FERTILITY

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Abstract

SOME REPRODUCTIVE PARAMETERS IN HUMAN FERTILITY

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Results of investigations made to obtain some reproductive parameters in human fertility are reported here. The data from a non-contracepting population in India with completed fertility have been used. It was found that the population's mean age at marriage was 17.7 years, and the mean ages at their first and last live births were 21.1 years and 36.8 years, respectively. In the reproductive life span of 19 years, the women had an average of five live births. The sex ratio at birth for families of all sizes was 100 males per 100 females. Couples who had children of both sexes at a specific parity tended to have a longer birth interval for the next live birth than those who had children of one sex. The incidence of primary sterility in the population studied was 5.1 percent. Birth intervals one-to-two and one-before-last were about equal but were longer (by 14.8%) than the intermediate birth intervals, while the last birth interval was the longest of all (about 5.8% longer than the birth interval one-before-last).

I. INTRODUCTION

The reproductive histories of women living in communities where no deliberate efforts have been made to control fertility provide a perspective on the pattern of family formation in a natural setting. The term "natural" setting has been used here in the context in which Henry used the term "natural" fertility--to indicate the absence of deliberate birth control (1). Such data permit demographers to estimate biological parameters in human reproduction within the social context of a country without the masking effect of deliberate controls. Some of the earliest data used for this purpose were from studies of groups of Hutterites in Canada and the United States (2-3). Recently, other surveys have been conducted in developing countries where there are almost no deliberate controls on fertility, and demographers have attempted to use these data to further explore the natural factors affecting human reproduction (4-6). This paper is also oriented to this goal. Data on the reproductive histories of women in an urban area in India who had married at an early age and used no method of fertility control are used to explore some aspects of human reproduction and to formulate estimates of some of them. While these data are limited to a particular population, the findings may be applicable to other non-contracepting populations as well.

II. MATERIALS AND METHODS

A fertility and family planning survey was carried out in 1974 in a railway colony in Kalyan near Bombay, India. The colony was inhabited by 5014 employees

forming an economically and educationally homogeneous group of generally lower middle-class families. Households with currently married women ranging in age from 15 to 55 years were questioned about their demographic and social backgrounds, their reproductive histories, and their family planning practices. Information was collected by physicians, hospital staff, and trained investigators who enjoyed a good rapport with the population and were responsible for providing health and family planning services to the community (7). This is a report based on a subset of these data; it focuses on the reproductive histories of women who had completed their reproductive lives without practicing any family planning method. The reproductive experiences of all women aged 35 years and over who had not been pregnant within at least three years prior to the survey and who had never practiced any method of birth control were analyzed. The age distribution of the 913 women who met these qualifications is given below:

Age group	Percent distribution (N=913)
35-39	42.1
40-44	29.7
45-49	23.1
50+	5.1

The reproductive pattern--age at marriage, age at first birth, ages at various birth orders and percent of reproduction achieved by different ages of the group under study--are given in Tables I through IV. About 25 percent of the women were married before the age of 16--the minimum legal age for marriage; another 25 percent were married after the age of 19, and 50 percent were between 16 and 19 years old at the time of their marriage. Women in this study had their first live birth approximately at age 21 (3.4 years after marriage) and

their last live birth at about the age of 37. About 40 percent of the women who had children had their first live birth before the age of 20. Thus, they had had, on an average, five live births in about 19 years.* (The average ages at other birth orders are given in Table III.) In this population, reproduction at early ages was the trend--15 percent of the total reproduction had occurred by the age of 20 (Table IV), 40 percent by 25, 50 percent by 26, and only 11 percent after the age of 35.

Information on age or birth order at the time of the last live birth is used to estimate the incidence of primary and secondary sterility. The length of successive birth intervals for women with different numbers of live births was used to search for a possible pattern in birth intervals at the beginning, middle, and end of reproductive life. The sex composition of children in families with different numbers of live births was used to test various hypotheses regarding sex ratio at birth and voluntary efforts of couples to achieve the desired sex composition in the family.

III. RESULTS

Change in Sex Ratio for Higher Orders of Birth

It is sometimes reported that at higher birth orders the sex ratio is favorable to females. This hypothesis was supported by a study on data from India (8). A test of this hypothesis was attempted from data in this study. The observed sex composition in families with different numbers of live births

*Only five live births in the total reproductive life for this non-contraceptive group may seem to be an underestimate, but the non-participation of this group in the existing family planning services may suggest that this group is of lower fecundity than the general population.

was compared with the expected composition obtained under the assumption that the sex of a child follows the binomial law of probability with a constant p (= probability that child is a male = 0.5). That is, the proportion of families with r (r = 0, 1, ...n) male and (n-r) female live births out of all families with n live births was obtained from the expression

$$\binom{n}{r} p^r (1-p)^{n-r} \quad \text{where } p = 0.5$$

and compared with the observed proportions of families with r male and (n-r) female live births. The observed and expected distributions were not found to be statistically different for any n (=1,2 ...8). Thus, the data under consideration suggest that there is a 50:50 chance for a birth to be a male or a female, and this is true for families of different numbers of live births. This ratio did not change even for higher orders of birth.

Effect of Sex Composition of Children at a Specified Parity of Mother on the Length of the Next Birth Interval

The data suggest that couples who have children of the same sex tend to have the next child more quickly. For couples whose first child was a female, the average interval before the second live birth was 3.7 years compared to 4.1 years for couples whose first child was male. For couples who had two live births, both of the same sex (males or females), the average interval for the next birth order was 3.1 years compared to 3.6 years for those who had one male and one female child. The same pattern persisted at higher (more than two) birth orders.

Sterility

Human fertility is affected both by socio-cultural and biological factors. Because the women in the population under study are quite young at the time of sexual union, they will probably go through a period of adolescent subfecundity, especially in the case of very early marriages. This pattern of adolescent subfecundity could not be estimated for this population because marriage did not always correspond to cohabitation. Some husbands left their villages to work in urban areas leaving their wives with parents or their families for varying periods of time.

The incidence of primary sterility* in the population was 5.1 percent. Despite exposure to reproduction early in life and making no effort to control pregnancy, 5.1 percent of the women studied did not bear children. This group was gradually joined by others who became sterile after one or more live births (secondary sterility). Both the age of the woman and the number of live births affect the incidence of secondary sterility. This analysis revealed the pattern of onset of secondary sterility as a function of both birth order (Table V) and age (Table VI).

About 29 percent of the women had two or fewer live births, 48 percent had three or fewer, and only 23 percent had more than five live births (Table V). The probabilities of becoming sterile at different orders of birth (1-A, A=parity progression ratio**) have also been computed and given in Table V. This probability increases with birth order, i.e. the higher the birth order, the higher

*Primary sterility denotes inability to give birth to a live baby. In contrast, secondary sterility refers to women who become incapable of bearing a child after one or more live births.

**The parity progression ratio is defined as the number of mothers who had at least $i+1$ live births divided by the number of mothers who had at least i live births.

the probability that a woman will not go to the next birth order. The probability of sterility at the second birth order is 0.190, a very sharp increase from 0.071, the probability at the first birth order. This sharp increase may suggest that a relatively subfecund group of women may manage to achieve at most two live births; this group constitutes about 29 percent of the population.

The crucial reproductive ages for women in this population were between 25 and 34 years (Table VI). About 40 percent were sterile by the age of 30 and 75 percent by 35. These percentages are even higher than those reported for pre-war rural Japan by Henry, who observed that the onset of sterility for Japanese women was generally much earlier than for European populations for whom data were available (1). This may be attributable to their smaller physical stature, possibly creating a higher risk at delivery, or the generally poor condition of their health.

Birth Intervals

Two dimensions of birth intervals investigated in this paper are the changing length of birth intervals from one birth order to the next, and the comparative length of birth intervals for women with different numbers of live births. The study of changing lengths of birth intervals in the absence of birth control measures assumes importance, since fecundity declines with age; consequently, the birth interval would tend to increase even if other components such as amenorrhea or gestation remain unchanged. This increase will be especially large toward the end of a woman's reproductive life. The comparative length of birth intervals for women with different numbers of births is indicative of the relationship between the length of birth intervals (which is a rough index of fecundity assuming other components are comparable in this homogeneous population), the length of reproductive life, and the number of children she bears.

For this purpose, the mean length of reproductive life and the length of the birth intervals between successive births were computed for groups of women with different numbers of live births (Table VII). The successive birth intervals beyond the first birth* show the following general patterns:

1. For women with a given number of live births, the intervals between the birth of the first and second (one-to-two), the penultimate (one-before-last), and the last child are generally longer than the other birth intervals, which will be called intermediate birth intervals.

2. Typically, birth interval one-to-two is equal to the interval one-before-last.

3. The last birth interval is the longest.

These general observations suggest relationships between successive birth intervals. The relationship between the three groups of birth intervals was obtained by two equations relating (a) intermediate birth intervals with birth interval one-to-two (or one-before-last), and (b) the birth interval one-to-two (or one-before-last) with the last. The former relationship was obtained from the last four groups of women (with five to eight live births) and the latter from the last six groups of women in Table VII. If L_o, L_1 and L_2 are defined as lengths of birth intervals for intermediate births, for birth interval one-to-two (or one-before-last) and for the last birth interval, respectively, the relationships are shown in the following expressions:

$$L_1 = (1.1475)\ L_o$$
$$L_2 = (1.0575)\ L_1$$

*The interval between marriage and first birth is composed of factors some of which are different from the ones which compose other birth intervals.

These expressions suggest that birth interval one to two (or one-before-last) is larger by 14.75 percent than intermediate birth intervals. The last birth interval is still longer and increases by 5.75 percent over birth interval one-before-last. These relationships are helpful in estimating or correcting L_0, L_1 and L_2 from known value of any of them.

The above equations were used to estimate the length of birth intervals for intermediate births for each group of women with different numbers of live births (Table VIII). The length of reproductive life as calculated from these relationships corresponds with the observed length (Table VIII). In this comparison, the first birth interval (zero-to-one) was excluded because different factors influence it. The features reflected in Table VIII are:

1. Women with larger numbers of live births have slightly longer reproductive lives and shorter birth intervals.
2. On the basis of the estimated length of the intermediate birth intervals, this population can be categorized into three groups--those who have two or fewer live births, those with three or four live births, and those with five or more live births. These three groups may be suggestive of the three fecundity groups in the population.

IV. SUMMARY

This paper reports data on the reproductive histories of women who had completed their reproductive lives without using any family planning method. The purpose was to explore the mechanism of human reproduction and to build estimates of some reproductive parameters. Women in this population married at a mean age of 17.7 years. Mean age at first live birth was 21.1 years and at

last live birth, 36.8 years. Thus, the average reproductive life span was about 19 years during which 5.0 live births occurred. The following are the important results:

1. The sex ratio at birth was 100 males per 100 females, independent of family size.

2. Couples who have children of the same sex at a specific parity tend to have a shorter birth interval for the next live birth.

3. The incidence of primary sterility in this population is 5.1 percent. This paper estimates sterility as a function of both age and parity. About 48 percent of the women had three or fewer live births, and only 23 percent had more than five live births.

4. Ages 25 to 34 are the crucial reproductive years among these women--about 75 percent of them became sterile by the age of 35.

5. Birth intervals one-to-two, one-before-last, and the last were longer than other birth intervals (intermediate births). The former two were about equal and the last one was longest. Quantitatively, the birth interval one-to-two or one-before-last was longer by 14.75 percent than the intermediate birth intervals. The last birth interval was longest--about 5.75 percent longer than birth interval one-before-last.

6. Women with higher numbers of live births have relatively longer reproductive lives and shorter birth intervals. If the birth interval for

intermediate births is taken as a rough index of fecundity (assuming other components like amenorrhea are comparable for all women), women in this population could be categorized into three groups--those with two or fewer live births, those with three or four live births, and those with five or more live births.

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TABLE I

DISTRIBUTION OF WOMEN BY AGE AT MARRIAGE

Age at Marriage	Percent Distribution of Women *(N = 913)*
12 or less	1.0
13–15	24.6
16	16.4
17	7.4
18	14.0
19	11.7
20	14.2
21 or more	10.8
Mean age at marriage (and standard deviation)	17.7 ± 3.0
Median age at marriage	17.5

TABLE II

DISTRIBUTION OF MOTHERS BY AGE AT FIRST LIVE BIRTH

Age at First Birth	Percent Distribution of Women *(N = 866)*
15 or less	8.7
16–17	16.2
18–19	16.3
20–21	18.1
22–23	12.8
24–25	10.2
26 or more	17.7
Mean age at first birth (and standard deviation)	21.1 ± 4.7
Median age at first birth	20.3

TABLE III

MEAN AGE OF MOTHERS (AND STANDARD DEVIATION) AT VARIOUS BIRTH ORDERS

Birth Order	Mean	S.D.
1	21.1	± 4.7
2	24.7	± 5.2
3	27.2	± 5.2
4	28.9	± 5.0
5	30.3	± 4.9
6	31.8	± 4.6
7	33.2	± 4.1
8	34.5	± 4.4
Last	36.8	± 3.7

Note: Only ages at the first eight birth orders and at the last one were considered.

TABLE IV

PERCENT OF TOTAL FERTILITY BY AGE

Age	Percent Reproduction	Cumulative Percent Reproduction
17 or less	7.7	7.7
18–19	7.1	14.8
20–24	25.6	40.4
25–29	27.6	68.0
30–34	21.5	89.5
35–39	8.8	98.3
40 or more	1.7	100.0

TABLE V
STERILITY BY BIRTH ORDER

Birth Order (n)	Proportion	Cumulative Proportion	Probability of Sterility*
0	0.051	0.051	0.051
1	0.067	0.118	0.071
2	0.168	0.286	0.190
3	0.189	0.475	0.265
4	0.168	0.643	0.320
5	0.125	0.768	0.350
6	0.097	0.865	0.418
7	0.061	0.926	0.452
8	0.039	0.965	0.527
9 or more	0.035	1.000	1.000

* *This column is the same as (1 — parity progression ratio).*

TABLE VI
STERILITY BY AGE GROUP

Age Group (x)	Proportion	Cumulative Proportion	Probability of Sterility
Primary sterility	0.051	—	—
19 or less	0.027	0.078	0.028
20–24	0.089	0.167	0.097
25–29	0.228	0.395	0.274
30–34	0.357	0.752	0.590
35–39	0.197	0.949	0.794
40 or more	0.051	1.000	1.000

TABLE VII

MEAN LENGTH OF REPRODUCTIVE LIFE AND LENGTH OF BIRTH INTERVALS IN YEARS BY NUMBER OF LIVE BIRTHS

Birth Interval	Number of Live Births							
	1	2	3	4	5	6	7	8
0–1[a]	5.8	4.5	4.0	3.3	2.5	2.5	2.4	2.3
1–2		5.1	4.1	3.8	3.3	2.9	2.9	2.9
2–3			4.3	3.7	2.8	2.6	2.4	2.4
3–4				3.9	3.2	2.7	2.5	2.4
4–5					3.4	2.9	2.7	2.2
5–6						3.1	2.8	2.5
6–7							3.1	2.8
7–8[b]								3.0
Mean length of birth interval	5.8	4.8	4.2	3.7	3.1	2.8	2.7	2.6
Mean age at effective marriage[c]	18.4	18.2	17.9	17.7	17.5	16.7	15.9	15.4
Mean age at end of reproductive life (sterility)	24.2	27.8	30.3	32.4	32.7	33.4	34.8	35.9
Mean length of reproductive life	5.8	9.6	12.4	14.7	15.2	16.7	18.9	20.5

[a] *Birth interval 0–1 refers to the interval from marriage to first birth. This interval should be considered separately from others since it includes, unlike others, a period of adoslecent subfecundity and does not include a period of amenorrhea.*

[b] *The study was limited to the first eight birth intervals because of the small number of women with more than eight children.*

[c] *The age at effective marriage is the age at cohabitation; this age may differ from the age at marriage.*

TABLE VIII

ESTIMATED BIRTH INTERVALS FOR INTERMEDIATE[a] BIRTHS, ESTIMATED AND OBSERVED LENGTHS OF REPRODUCTIVE LIFE BY NUMBER OF LIVE BIRTHS

Parameters of Reproductive Life	Number of Live Births						
	2	3	4	5	6	7	8
Estimated birth intervals for intermediate births	4.2[c]	3.6[d]	3.3[f]	2.8	2.5	2.5	2.5
Estimated length of reproductive life[b]	5.1	8.4[e]	11.5[g]	12.7	13.9	16.2	18.6
Observed length of reproductive life[b]	5.1	8.4	11.4	12.7	14.2	16.5	18.2

[a] *Data in TABLE VII showed that successive birth intervals for a given group can be grouped into three categories — birth interval 1—2 or one-before-last, last and the others. The term "intermediate birth intervals" has been used to refer to the last category, i.e., "others".*

[b] *From first birth to last birth.*

[c] *From the two equations given in the text, $L_2 = (1.21)L_0$. L_0 was computed for the value of $L_2 = 5.1$.*

[d] *The relationship $L_1 = (1.1475)L_0$ was used to get L_0 for $L_1 = 4.1$.*

[e] *The relationship $L_2 = (1.0575)L_1$ was used to get L_2 for $L_1 = 4.1$. The sum of L_1 and L_2 is equal to 8.4.*

[f] *For all groups with 4 through 8 live births, estimated L_0 was obtained from $L_1 = (1.1475)L_0$ where L_1 was average of birth interval 1—2 and of one-before-last.*

[g] *The estimated length of reproductive life for all groups with number of live births 4 through 8 was obtained from expression $2L_1 + L_2 + (n-4)L_0$ where L_0 is estimated as in "f" above, L_2 is estimated by equation $L_2 = (1.0575)L_1$ and n corresponds to the group of women with n number of live births.*

E

NEWER DEVELOPMENTS IN FEMALE METHODS OF FERTILITY CONTROL

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INTRODUCTION

Because of several sociologic and technological developments over the past decade, efforts to develop better methods of fertility control have become increasingly important. First, information about and access to methods of fertility control have become recognized as basic human rights. Second, the liberation of women from social and legal inequality has rapidly opened occupational and cultural opportunities for them outside their traditional role of childbearing. Third, there is an increasing awareness of the pressures of population on limited world resources. Fourth, leaders of major developing countries have come to realize that high rates of population growth and low per capita income are incompatible with their aspirations for social structures that meet the basic needs of all their people. And finally, it is becoming increasingly apparent that grand-multiparity and births at the extremes of reproductive life account for a major part of maternal and child morbidity and mortality. It is little wonder that birth planning has become an acceptable area for study and social action.

There have been important advances in methods of fertility control for female use, but in marked contrast, there have been almost no advances in methods for male use. Whether this is due to a lack of resources directed toward developing improved male methods, the existence of simple and effective methods such as the condom and vasectomy, or the more complex and less understood endocrine system

of the male is still debated. In most societies it is the female partner who first seeks family planning advice, and the fact that only women become pregnant remains a compelling argument favoring female methods of fertility control.

The demand for the principal fertility control modalities is illustrated schematically in Figure 1. The most desirable modality is shown as menstrual regulation, or treatment of the missed menstrual period within approximately two weeks of a missed menstrual period. It is desirable because it requires no planning, it is independent of coitus and is used only when needed--about four times each year. If a safe and effective oral medication for menstrual regulation is found, all of my further discussion will become as irrelevant to the practice of medicine as is salmonella typing and tuberculosis sanitaria today or smallpox vaccination tomorrow.

This review of newer developments in female methods of fertility control will progress from the least to the most acceptable modalities.

PERIODIC ABSTINENCE

Periodic abstinence, also referred to as the rhythm method or natural family planning, is based on the fact that ovulation occurs only once a month and the life of the sperm and the ovum is limited

to a few days. Research has been directed toward more accurately identifying this short fertile period.

Because of variability in the time of ovulation, and possibly in the fertile life of the ovum and sperm, a calendar approach alone leads to a lengthy period of abstinence for effectiveness. The recommendation of Ogino and Knaus, who separately discovered the mid-cycle fertile period in the 1930s, was to plot the average cycle length and abstain from intercourse three days before and after the assumed midcycle day of ovulation. This recommendation has not proven effective (1).

The addition of individual symptoms, such as "Mittelschmartz" and the recording of individual cyclic thermal patterns of basal body temperature has led to the "sympto-thermic" rhythm method, which is reported to improve efficacy for shorter periods of abstinence (2). Independent studies to confirm these reports are in progress (3).

The changing composition of cervical mucous throughout the menstrual cycle is a well known phenomenon and its measurement was advocated by Drs. Evelyn and John Billings in the 1960s as a way of predicting the fertile period and identifying the "safe" period of the menstrual cycle (4). More recently Kosasky at Harvard has developed an instrument (Ovutimer™, Ovutime, Inc., Chestnut Hills, Mass., USA) to measure the viscosity of cervical mucous (5-9). A

probe is used to collect a few milligrams of cervical mucous which is placed in the instrument. The lowest viscosity of cervical mucous occurs 12-18 hours before ovulation according to Kosasky.

Failure rates reported in studies of periodic abstinence vary greatly (10). Some of the more recent studies using measurement of viscosity of cervical mucous, with or without basal body temperature, indicate use-effectiveness failure rates of approximately 15 to 25 per 100 woman-years of use with a theoretical effectiveness as low as 2.9 (11-14). Whether the newer viscosity measuring instruments will provide use-effectiveness nearer the theoretical remains to be seen.

The Groden Method attempts to regulate the time of ovulation by administering oral contraceptives during the second half of the menstrual cycle (15-16). The method is being tried in the Philippines where 14 iron pills are taken one a day starting on the first day of the menstrual cycle followed by 11 daily contraceptive pills (17). Abstinence is recommended on days 11 through 18. Studies of Lorenzo and Sturgies, however, suggest that abstinence should be practiced from day 10 through 19 for high effectiveness (18).

Newer research is attempting to identify chemical compounds of saliva and cervical mucous throughout the menstrual cycle. These seem to have potential, but none are ready for use (19-22).

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Reports that the risk of abnormality among their offspring is higher for women using periodic abstinence are of concern, and this problem should be studied further (23-25).

The present methods using periodic abstinence are difficult to practice and have unacceptable failure rates, especially for couples who have completed their families. More sophisticated instruments to measure viscosity of cervical mucous might improve efficacy, but at considerable cost. However, ongoing research may yet produce a simple, effective, and inexpensive chemical "litmus paper" type test.

BARRIER AND SPERMICIDE METHODS

Interest in barrier and spermicide methods of contraception has recently been renewed. In Western, urban communities the increased use of the diaphragm is attributed to publicity and to the genuine concern of physicians and patients about side effects of IUDs and oral contraceptives (26, 27). The greatest increase in the use of these methods, however, has come from expanded distribution systems including distribution through such retail outlets as grocery stores in urban communities and through community-based distribution systems that are frequently subsidized as a form of social marketing in rural areas (28,29). Barrier and spermicide methods are particularly attractive to the growing group of unmarried persons who are sexually active only intermittently.

In addition to eliminating concerns about side effects of other contraceptive methods, the barrier and spermicide methods may also contribute to the control of sexually transmitted diseases. The present pandemic of gonorrhea is alarming and may even result in a new form of involuntary fertility control.

Barriers

The condom is anatomically a male method, but recent marketing practices have been directed toward purchases by women. This includes colors of the condoms, packaging design, and choice of retail sales outlets. No doubt in some cultures the male's active role in condom contraception is limited to removal of the condom after use.

While the condom is theoretically as effective as the IUD--about 2.4 failures per 100 woman-years of use--its actual failure rate is generally thought to be two to three times higher (30).

Newer developments in manufacturing condoms incorporate the use of thinner materials of both latex and plastic composition and prelubrication packaging. Marketing patterns would indicate that these have been desirable innovations (31).

The diaphragm has not changed in many years and remains a reliable, but difficult method to use. Two recent studies in urban clinics of Western countries indicate failure rates under 3 per 100

woman-years of use (32, 33). A similar device, the cervical cap, has been popular in England for many years and is comparably effective. Recently a flexible plastic cap has been produced which may be both less expensive to produce and resistant to deterioration caused by heat, acidic vaginal fluid or oil-based spermicides. Both the diaphragm and cervical cap must be fitted by professional personnel and this remains a major constraint to their wider use.

The use of sponges as vaginal barriers is not new, but this method has never been carefully evaluated. In the 1950's a rubber sponge moistened with saturated salt solution was used (34). Burnhill tried urethane sponges, but was not satisfied with their ability to block sperm (35). More recently Vorhauer has developed newer models of a urethane sponge incorporating a spermicide that are in early clinical trials (36).

Perhaps the most interesting innovation has been the development of the collagen sponge as a vaginal barrier. Chvapil and colleagues report that the collagen sponge is so well tolerated that it can be left in place between menstrual periods (37, 38). Odors related to decomposition of sperm do develop. These can be reduced by rinsing the sponge in water or by adding zinc to the sponge. Its use as a menstrual tampon is also being investigated. The addition of both spermicidal and bacteriocidal agents will also be tried.

The fact that collagen is a natural substance possibly accounts for its reported low incidence of irritation in the vagina. Its high fluid binding capacity may contribute to the trapping of sperm within the sponge. Larger trials of both the plain and zinc collagen sponges are planned. The sponges are packaged pre-moistened so that they are soft and ready to use. No special fitting of the sponge is necessary.

Spermicides

Vaginal foams, creams and jellies have been used alone or together with the diaphragm. They consist of an inert base designed to block sperm and active spermicidal agents. Mercury and hydroquinones were used in earlier preparations, but fear of toxic effects has lead to the use of safer compounds with a surface active principal capable of disrupting the sperm cell walls. Two surfactants in common use are p-methanylphenylpolyoxyethylene and nonoxynol-9. Most of the applicators for the creams, jellies, and foams are tampon-shaped, either re-useable or disposable. Foaming tablets are manufactured in Japan, Germany, Belgium, and the U.K. and a water soluble plastic film is available in Europe.

However, vaginal spermicides used alone have relatively high failure rates. Although it has been claimed that their effectiveness is less than five pregnancies per 100 woman-years of use, reported use-effectiveness rates are as high as 35 per 100 woman-years of use (26). The National Fertility Survey in the USA

reported that 31 percent of the women using foam had an unplanned pregnancy in the first year of use, compared to 6 percent of those using the pill and 8 percent of those using IUDs (39).

In spite of the slow development in barrier and spermicide contraceptives, recent developments in social marketing of these methods and recent combined private and public support for developing an effective and acceptable sponge, make the prospects for expanded use of these methods very good indeed.

INTRAUTERINE DEVICES

Intrauterine devices (IUDs) are an attractive alternative to other methods of contraception. That this method is coitus independent, requires only one simple and safe procedure to initiate contraception, and most devices cost little to manufacture are compelling arguments for its widespread use. However, except in a few areas the proportion of contraceptors choosing the IUD remains relatively small (40). Side effects and inadequate delivery systems have prevented realization of the full potential of this method.

Graefenberg gave his first report on the Graefenberg Ring in 1931 (41). However, the method fell into disrepute as a generation of textbooks warned of the dangers of infection associated with the use of IUDs. It was only after Oppenheimer's reassessment in 1959 that

IUD research and development became active again (42). Lippes (43) presented his experience with the Lippes Loop (Figure 2) in 1962, and by 1970 Tietze and Lewit could report from the Cooperative Statistical Program for the evaluation of IUDs on the use of 10 inert devices for a total of 23,917 insertions and 469,217 woman-months of use (44).

In the late 1960s reports of two medicated IUDs appeared. Zipper and colleagues demonstrated the effectiveness of copper (45) and Scommengna showed the effectiveness of progesterone (46) in reducing pregnancy failures when copper ions and progesterone are released from small IUDs. Both the Copper T and Copper 7 IUDs (Figure 3), both with 200 mm^2 of copper wire, are now approved by the US Food and Drug Administration (FDA) for 36 months of use. The actual release of copper ions is negligible in the second and third years, and the exact mode of action of copper ions is unknown (47). The FDA approved the Progesterone T (Figure 4) which releases 65 μg of progesterone per day for at least 1 year. Three-year devices are being developed (48).

Performance differences among the Lippes Loop, Copper T, Copper 7, and Progesterone T can be summarized as follows. Their failure rates are similar in the first year--about 3.2 pregnancies per 100 woman-years of use (44, 49, 50). The Progesterone T is not approved for the second and third years of use. By the second year of use (51) the Lippes Loop has a cumulative failure rate of 5.5 and the

Copper T of 6.1. However, a variation of the Copper T (Cu-T-220) with copper cyclinders on the horizontal arms, which is not yet generally available, has a failure rate of only 2.0 at the end of the second year (52). The bleeding patterns of the three devices are well established and quite different. The Lippes Loop causes the heaviest menstrual bleeding--about twice the normal menstrual blood loss. The Copper T and Copper 7 devices cause about a one third increase in menstrual blood loss (53, 54). The Progesterone T actually reduces menses to about half of the normal blood loss. However, use of the Progesterone T is associated with more frequent intermenstrual bleeding than the use of either the Lippes Loop or the copper devices. This intermenstrual bleeding declines over the first 3 months of use of the Progesterone T (55). Expulsion rates are similar (ranging from 5 to 10 per 100 woman-years of use) for all of these devices. A distinct advantage of the Lippes Loop and other inert devices is that they may be safely used for an indefinite period of time.

There is no evidence to date of teratogenic effects of either copper or progesterone on the offspring of women who conceive while using this method (56, 57). However, reliable data are available only for copper; the use of progesterone, other steroids or antifibrinolytic agents must be carefully monitored (58, 59).

Epidemiologic studies have explored the risks of IUD-associated infections, abortions, septic pregnancies, and perforations. Retrospective case-control studies indicated a more than threefold risk

of pelvic infection in IUD users among patients treated in outpatient clinics (60-62). The estimated incidence of IUD-related infections that required hospitalization in 1973 in the United States was 5 per 1000 women-years of use (63). The importance of the present rising incidence of gonorrhea among successful IUD users is not clear and is a matter of concern (64). Copper does not appear to offer protection against gonorrhea infections (65).

The risks of spontaneous abortion for women who conceive while using IUDs is thought to be about 50 percent, or three times that for the general population (66). Concern about septic abortion among IUD wearers is diminishing, however, as increasing evidence points to a marked decline in septic abortions among IUD users since the Dalkon Shield was removed from the market (67).

The IUD protects only against intrauterine pregnancy. Ectopic pregnancies, which have an expected incidence of 1 in 200 pregnancies in the general population, occur among IUD wearers as well. Recent evidence shows, however, that the rate of ectopic pregnancies among IUD users increases in the second and third years of use, possibly because of an increased incidence of pelvic infection among IUD users (57).

The incidence of IUD perforations reported in different studies varies from 1 in 120 to 1 in 2000 insertions. While it is generally

agreed that when perforation occurs copper IUDs should be removed because of the inflammatory response they cause in the peritoneal cavity and the risk of adhesions and subsequent bowel obstruction, the advisability of removing inert devices has not been established (68). Recommendations must be related to the varying risks in different settings of the procedure (usually laparotomy) used to remove the device. This risk may decline as more centers develop laparoscopic methods of removing perforated IUDs.

In spite of the limitations of present IUDs and the evidence of occasional serious complications associated with their use the death rate attributable to IUD use is low when compared with the risk of death associated with childbirth. The risk-benefit ratio of IUD-related deaths to births averted is lower than the corresponding ratios for oral contraceptives or condoms/diaphragms (69). The challenge to IUD research is to find an IUD design that will reduce the most troublesome side effect--increased vaginal bleeding. There is also need for a device design that will improve retention for postpartum insertions.

The difficulty in designing an IUD that will minimize bleeding is illustrated in Figure 5; there is an inverse relationship between the surface area of inert IUDs and pregnancy failures, but there is direct relationship between surface area and IUD removals for pain and bleeding. One successful approach to the dilemma has been to

add medicants, such as copper or progesterone, to small IUDs such as the Copper T and 7 to improve efficacy. Another approach now being investigated is to add medicants, such as AMCA and progesterone, to an effective, high surface area device such as the Spring Coil to alleviate bleeding (Figure 6). Ragab was the first to conduct clinical trials of an AMCA-releasing device (70). He used the U-coil, which is a variation of the Spring Coil. The marked reduction in removals for pain and bleeding for the AMCA-releasing U-coil compared to a copper ion releasing U-coil is show in Figure 7. Hefnawi studied quantitative blood loss in a progesterone-releasing Spring Coil (71). His results, illustrated in Figure 8, show a considerable reduction in bleeding attributable to progesterone; postinsertion menstrual blood loss is even lower than preinsertion levels. As with the Progesterone T, however, intermenstrual bleeding was slightly increased. The release of antifibrinolytic agents using modified Copper T and Lippes Loop IUDs as carriers is also being investigated.

The only device, other than the Spring Coil, that has been reported to have a near-zero pregnancy rate is a zinc- and copper-clad 7-shaped device being investigated by Zipper (72). Further work is needed to document the safety of zinc when released in the uterine cavity.

Progress has recently been made in the development of a design for immediate post-placental insertions. The Lippes Loop was first

modified (Figure 9) with the addition of silastic tines which would extend in the anterior posterior direction on the superior arm of the Loop. Table I shows improved 3-month rates of expulsion for this modification (73). A more recent modification, biodegradable extensions in the form of chromic sutures (Figure 10), also appears encouraging (74).

A neglected approach to improving IUD use-performance is to select the IUD most appropriate for a particular woman (75). It has been known for some time that rates of pregnancy, expulsions, and removals for pain and bleeding for IUDs vary among women with different characteristics. Some of the more important biological characteristics determining IUD performance are age and parity, number of previous abortions, and internal os to fundus length of the uterus. It should soon be possible to prescribe a specific available IUD for a woman with a particular set of characteristics.

SYSTEMIC CONTRACEPTION

The combination estrogen-progestogen oral contraceptives are by far the most commonly used systemic contraceptives among the estimated 55 million women using this method of contraception. Since their introduction in the 1960s there has been a gradual reduction in the steroid dosage, and a remarkable variety of dosages are available today. While early dosage reductions were definitely warranted, it is estimated by Mackey and co-workers (76) that

preparations containing less than 30 µg ethinylestradiol and 150 µg d-norgestrel or their equivalent will result in lower contraceptive effectiveness and increased breakthrough bleeding. Whether this is true for all racial groups and women of widely different body weight remains to be seen. It is known that racial groups have different metabolic changes in response to oral contraception and that some side-effects of oral contraceptives tend to diminish for overweight women (77, 78). However, carefully controlled, comparative studies of different doses of oral contraceptives in varying population groups have not been reported.

A recent double-blind crossover study in the US comparing symptoms associated with the use of three widely used oral contraceptives showed interesting differences among the three preparations, Ovral (norgestrel 0.5 mg and ethinyl estradiol 0.05 mg), Norinyl (norethindrone 1 mg and mestranol 0.05 mg) Norlestrin (norethindrone acetate 1 mg and ethinyl estradiol 0.05 mg) (79). The lowest breakthrough bleeding was seen with Ovral, but Ovral had the highest incidence of nausea. Norinyl users reported the highest incidence of breast discomfort. Figure 11 shows the pattern of intermenstrual breakthrough bleeding when users of each oral contraceptive were switched to the other. Switching from Ovral to either Norinyl or Norlestrin resulted in increased breakthrough bleeding, and switching from either Norinyl or Norlestrin to Ovral resulted in decreased breakthrough bleeding, while little difference was noted in switches between Norinyl and Norlestrin.

The same study provided information on the probability of breakthrough bleeding when a tablet in a cycle was missed. For eacl of the three oral contraceptives, the probability of intermenstrual bleeding was increased about 15-fold by omission of a tablet (80).

It is recognized that many metabolic changes are brought about by steroidal contraception; most are transient and of apparently no clinical significance (81). Some serious, but rare, complications are associated with oral contraceptive use; the most studied of these is thromboembolism. The risk of thromboembolic disease can be markedly increased by the presence of predisposing factors such as hyperlipoproteinemia, cigarette smoking, and hypertension (82). Smoking appears to be the greatest additional risk factor (83-85).

Study of the association between neoplasia and oral contraceptive use suggests that it may protect against benign breast tumors; there is no evidence of an increased risk of malignant breast tumors (86-91). While sequential oral contraceptives are suspected as a cause of endometrial cancer, there is no proof of a causal relationship (92). This suspicion and their higher estrogen content prompted the US Food and Drug Administration (FDA) to remove sequential contraceptives from the market in 1976. Oral contraceptives, especially those containing mestranol, have also been linked to an increased incidence of benign hepatoma. Evidence linking oral contraceptive use to the few malignant cases is lacking (93-97).

Considerable concern has been expressed about the risks associated with oral contraceptive use. Because of their contraceptive efficacy, however, the risks must be assessed in terms of the alternative methods and the risks of contraceptive failures, including abortion and childbirth. When analyzed in this manner, as in studies by Teitze et al. (98) and Potts et al. (99), oral contraception has a satisfactory risk ratio, compared with those of other contraceptive methods, in the absence of conditions that predispose to increased risk of thromboembolic disease. When these conditions are present, women over 35 years of age should consider other contraceptive methods. Of course, anyone who smokes should be advised to give it up, but especially women taking oral contraceptives.

Of the progestogen-only steroidal contraceptives, the mini-pill formulations have not seen widespread use, possibly because of poor cycle control and lower effectiveness. They have been recommended for breastfeeding women on the assumption that they interfere less with lactation than combination estrogen-progestogen formulations. There is need, however, for studies of the effect of different progestogens on lactation. The long-acting injectable, medroxy-progesterone acetate, (Depo Provera, The Upjohn Company, Kalamazoo, Mich., USA), has been found highly effective in doses of 150 mg given every 3 months or 300 mg given every 6 months (100). The use of subdermal implants and vaginal rings for the delivery of steroidal contraception is still in the clinical trial stage (101).

One of the most exciting developments in oral contraception relates not to new formulations or routes of administration, but to new delivery systems of presently available oral contraceptives. The community-based distribution (CBD) of oral contraceptives by community leaders in rural areas of developing countries has made this excellent contraceptive available to a neglected group in greatest need. The rationale for this non-medical distribution is that the overwhelming majority of women in need of a medical examination before starting oral contraception can be identified by history alone (102). CBD programs commonly use a check-list of questions such as the following.

1. Yellow skin or eyes _____ _____
2. Breast mass(es) _____ _____
3. Watery or bloody discharge from the breast (nipple) _____ _____
4. Abnormal menstrual periods or frequent vaginal bleeding _____ _____
5. Vaginal bleeding after intercourse _____ _____
6. Swollen and/or painful legs _____ _____
7. Severe chest pain _____ _____
8. Weakness or shortness of breath after exertion _____ _____
9. Frequent, severe headaches _____ _____
10. Varicose veins _____ _____
11. An infant three months old or less which she is breast feeding _____ _____
12. Is the woman over 40 years old and does she smoke cigarettes _____ _____

If all answers are negative, the woman is provided oral contraception without medical consultation. The initiation of these newer distribution systems accounts in part for the continued increased use of oral contraception in developing countries. There is also an increasing concensus of medical opinion that oral contraceptives may be safely distributed by non-physicians in developed countries as well (103).

FEMALE STERILIZATION

It is estimated that sterilization is now the most prevalent means of fertility control. Table II shows the remarkable increase in reliance on this method in this decade. The completion of desired family size early in reproductive life and the improvements in techniques of female sterilization account for this increase. Female sterilization can now be safely performed on an outpatient basis. Sterilization is about equally divided between men and women at this time, but the proportion of female sterilizations is rising (104, 105).

Female sterilization methods may be categorized in terms of approach to the Fallopian tubes (laparotomy, laparoscopy, colpotomy, culdoscopy, hysteroscopy, blind transcervical), by pregnancy status of the patient (interval, postpartum, postabortion), and various techniques of occluding the Fallopian tubes (ligature, electrocoagulation, clips, rings, chemicals, plugs). These options are summarized in Table III.

Both the approach to the Fallopian tubes and the method of occluding the tubes are in a period of intense development; it is difficult to predict what the situation will be by the end of the decade. Careful comparative studies

will be needed to document the superiority of one approach or technique over another in various clinical settings.

The safest and most economical method of female sterilization remains laparotomy and ligation for postdelivery patients, but at the same time, this combination is rapidly disappearing for interval and postabortion patients. For these patients laparoscopy has been the preferred method, but it is now being challenged by a variation of laparotomy known as minilaparotomy. Minilaparotomy was described in 1965 and 1969 and was popularized more recently by Vitoon. It is an outpatient procedure requiring only local anesthesia. The key elements in the surgical technique are as follows: a small suprapubic incision of generally less than one inch; specially designed retractors to permit visualization of the tubes; uterine elevators, suction cups, or digital manipulation to move the uterus toward the anterior abdominal wall for easier access to the tubes; and tubal hooks or Babcock forceps to retrieve the tubes. The tubes may be drawn through the incision and ligated or occluded within the pelvis with a specially designed tubal ring or clip applicator (106-108). The application of tubal rings in minilaparotomy sterilization is shown in Figure 12. Figure 13 shows an example of a kit of specialized instruments for minilaparotomy.

Laparoscopic sterilization is widely accepted by both patients and surgeons. It has definite advantages over minilaparotomy in obese patients. The method involves pneumoperitoneum; insertion of a trocar, cannula, and laparoscope through a small abdominal incision; uterine manipulation with an intrauterine elevator; and occlusion of the tubes through an operating laparoscope or through a second incision. The steps are shown in Figure 14.

Electrocoagulation with monopolar forceps was the first technique used for tubal occlusion. Infrequent but serious complications occurred in the form of bowel burns (109). Bipolar forceps for electrocoagulation were introduced in the hope of minimizing this risk, but its safety and effectiveness are still unproven. The extensive tubal damage and accidental injuries caused by electrocoagulation have led to development of a thermocoagulation method consisting of a hot wire hook in a protective teflon sheath (110), as shown in Figure 15. The trend now, however, is away from electrical techniques of tubal occlusion as experience is gained in nonelectrical techniques.

The spring-loaded clip (Spring-loaded Clip, Richard Wolf Medical Instruments Corporation, Rosemont, Ill., USA) developed by Hulka and Clemmons (111, 112) and the tubal ring (Falope Ring, KLI, Newtown, Penn., USA) developed by Yoon (113, 114) have each been studied using single-incision operating laparoscopes. The occlusive devices and applicators are illustrated in Figures 16-19. Because it is applied across the tube, the clip is less destructive to the Fallopian tubes. The tubal ring produces a Madlener type occlusion, using a silastic band instead of suture, as shown in Figure 20. The relative failure rates of the prototype clip, ring, and electrocoagulation in laparoscopic sterilization are shown in Figure 21. The 12-month life table rate for electrocoagulation of 0.2 per 100 woman-years of use represents eight cases of which three were ectopic pregnancies. There were no ectopic pregnancies in this series for the clip or ring (115).

Other promising nonelectrical occlusive techniques for laparoscopy or minilaparotomy have not been fully evaluated. These include the Bleier clip shown in Figure 22 which is made of plastic (116). A variation of the spring-loaded clip using a second incision applicator (Rocket of London, Watford, England) is being investigated (117).

Family Research Program (IFRP) on 8,500 laparoscopic sterilizations and 2,820 minilaparotomy sterilizations show both methods to be safe and effective (115). The results are summarized in Table IV. There appears to be no definitive advantage of one approach over the other. In developing countries with limited resources, especially those where women tend to be thin, minilaparotomy seems the method of choice. However, there are indications that laparoscopic sterilization is more acceptable to women in rural areas of India (118, 119), and this fact, combined with the prospect of more durable and less expensive equipment for laparoscopic sterilization, may justify laparoscopic sterilization programs in less developed countries in the future.

Recently, there has been considerable improvement in optics designed for miniaturized endoscopes. Figure 23 shows a miniaturized laparoscope of 2.7 mm diameter that provides adequate visualization of the Fallopian tubes. A bipolar electrocoagulation forceps has been developed to pass through a 3 mm cannula, but it is not yet commercially available. The equipment has been used in rural areas of India where the idea of a "needle puncture" technique of female sterilization would be very attractive (120).

Both colpotomy and culdoscopy are associated with higher rates of complications, especially infections, than laparotomy, laparoscopy, or minilaparotomy (121-124). Studies to assess the application of tubal rings by both approaches are in progress. However, it seems unlikely that these approaches will prove superior to minilaparotomy, although they may be more acceptable to some pateints and physicians.

Hysteroscopic sterilization by electrocoagulation or instillation of quinacrine has been disappointing in that it is associated with high failure rates and, in the case of electrocoagulation, with serious complications (125-127). The hysteroscopic application of intraluminal plugs, tissue glues, or liquid silastic is being investigated, but none of these procedures are ready for large clinical trials (128-132).

Cryosurgery of the endometrium in the area of the uterotubal junction is under active investigation as a sterilization method (135).

The search for a nonsurgical method of female sterilization continues. Zipper has pioneered this approach using repeated transcervical instillations of quinacrine alone and quinacrine with various adjunctives (133, 134). Reports of studies done to date indicate that the efficacy of this method is not yet acceptable, but the approach has considerable potential.

Richart and co-workers have developed an efficient blind transcervical delivery system for methyl 2-cyanoacrylate (MCA) that appears to cause reliable and permanent tubal fibroses (136, 137). The delivery system is shown in Figure 24. A balloon occludes most of the uterine cavity. Then, a measured amount of MCA is delivered to the uterotubal junction. Further inflation of the balloon pumps the MCA into the Fallopian tube. The method is in early clinical trials.

An exciting immunologic approach to female sterilization is being investigated by Talwar and co-workers (138). They have linked beta subunit fragments of HCG to tetanus toxoid as an adjuvant causing antibody response to HCG and temporary sterility in animals. Human trials to monitor antibody titers and possible

side effects among sterilized volunteers are in progress (139). It will take a number of years, at best, to perfect this method. It could, however, revolutionize present practices in female sterilization.

A remarkable increase in demand for female sterilization has accompanied the development of simpler and safer outpatient procedures. Minilaparotomy is ready for very broad application and nonelectrical laparoscopy techniques should soon be available in major medical centers. While prospects for a nonsurgical method of female sterilization appear good in the next several years, the primary challenge at this time is to make available the excellent surgical procedures which have already been developed.

ABORTION

Abortion is a very old method of fertility control. When performed outside of modern medical facilities, the procedure can be dangerous and expensive. When abortion is legalized for liberal indications and made generally available, there is a marked increase in abortion services and a definite drop in infant mortality (140), maternal mortality (141), and the number of babies available for adoption (142). The high cost of treating incomplete abortions in Latin America has been well documented (143) and is obviously related to present restrictive abortion laws.

When abortion services are first made available, the tendency is toward a high proportion of requests for midtrimester abortions (144). As information about services and prompt availability of services improves, the proportion of requests for midtrimester abortion declines. The demand for first trimester abortions, and especially repeat abortions, depends on the quality of contraceptive

services (145). But contraceptive services are far more difficult to provide to unmarried teenagers than to mature married couples. This in large measure accounts for the high abortion-to-birth ratios in most parts of the United States where approximately 50 percent of the abortions are requested by unmarried women and the modest ratios in a country like Singapore, where over 95 percent of the requests are from married women, and a high proportion of these requests are prompted by contraceptive failures (146).

First trimester methods

Vacuum aspiration is the method of choice for first trimester abortion (147). The procedure can be safely performed on an outpatient basis without general anesthesia. Paracervical block is frequently used for nulliparous women and analgesia only for parous women. Prophylactic antibiotics are generally not used where the patient can be easily followed up. However, a study by Hodgson et al. (148) has shown that use of oral tetracycline hydrochloride 1.5 g preceding vacuum aspiration followed by 500 mg every 6 hours for 4 days can reduce febrile complications from 9.0 percent to 3.2 percent. Other clinics have had an incidence of febrile complications of approximately 3 percent without the use of prophylactic antibiotics (149). Meticulous care to assure complete evacuation of the uterus is probably the key to reducing febrile complications.

A significant proportion of the complications associated with first trimester abortion, such as perforations and cervical tears, are attributable to cervical dilatation (150). The long-term effects of cervical dilatation are unknown, but it is suspected that repeated dilatation beyond 9 mm could lead to cervical incompetence and premature labor in subsequent births (151).

Hulka et al. (152) measured the force required to dilate the cervix in first trimester abortions and found that Hegar dilators required more force than Pratt dilators. The maximum resistance was at 9 mm, and they concluded that there was tearing of the internal os rather than stretching of cervical tissues at this point. The soft plastic Karman cannula may require less cervical dilation than sharp curettage or a metal cannula and thus reduce complication rates associated with cervical dilatation (153).

Several alternative methods of cervical dilatation have been used. Laminaria tents have several disadvantages: they cause pain at insertion and take hours to act. Not only are the logistics of an efficient outpatient procedure made difficult by this time delay, but the possibility of introducing infection is a concern (154).

Pharmacologically induced dilatation of the cervix using prostaglandin analogues has been reported (155). Vaginal suppositories containing 15 (S)-15 methyl prostaglandin $F_{2\alpha}$ methyl ester and intracervical injections of 16,16-dimethyl prostaglandin E_2 benzaldehyde semicarbazone ester have been used. When given 3 to 4 hours before vacuum aspiration for first trimester abortion, these prostaglandin analogues produced adequate dilation in 75 percent of the patients (156). Carefully controlled comparative studies of these methods of cervical dilatation will be required, but this pharmacologic approach appears to have excellent potential, especially as improved analogues of prostaglandin are developed.

Second trimester methods

In contrast to the relatively low complication rates of first trimester abortion, complications from all methods of second trimester abortion are significant (Figure 25). Hysterotomy has been abandoned in most countries because of high complication rates. The intraamniotic instillation of pharmacologic agents is now the most frequently used method. Two accepted agents are hypertonic saline and prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$). Saline is frequently augmented by intravenous oxytocin (157) and/or intracervical laminaria tents (158).

Comparative studies with random allocation of subjects between unaugmented intraamniotic instillation of hypertonic saline and two doses of $PGF_{2\alpha}$ were conducted by the IFRP (159). The dose schedules included 20 percent sodium chloride, a single 50 mg instillation of $PGF_{2\alpha}$ and multiple instillation of 25 mg of $PGF_{2\alpha}$. The multiple-instillation prostaglandin schedule resulted in the shortest instillation-to-abortion time, while the saline group had the longest mean abortion time (Figure 26). The rates of major complications were not significantly different for the three groups, but hemorrhage and infections were more frequent with the saline method, while cervico uterine injuries were more frequent with the prostaglandin methods.

Recently, hypertonic urea was approved by the FDA for intraamniotic instillation. When augmented with small doses of $PGF_{2\alpha}$, it gives satisfactory results and is probably safer than saline (160).

It has been common practice in 13 and 14 menstrual week gestations to wait until the 15th week and perform intraamniotic instillation. Brenner and Edelman in analyzing IFRP pooled data were the first to suggest it may be safer to induce early second trimester abortion by dilatation and curettage (161).

Recent reports by Cates et al. analyzing data of the Center for Disease Control (CDC) confirm this (162). Their data actually suggest that dilatation and curettage may be safer than intraamniotic instillation of saline or $PGF_{2\alpha}$ up to 20 weeks' gestation (Figure 27). There are, however, few centers in the US that perform dilatation and curettage procedures after 16 weeks' gestation. The procedures are generally performed on an outpatient basis. In this regard they have an advantage over either intraamniotic instillation or multiple applications of prostaglandin analogues by intramuscular injection or vaginal suppositories (163).

A number of studies of long-term sequelae of induced abortion are in progress that may answer questions related to effects on future reproductive functions. The evidence suggesting increased prematurity is not substantial at present (151). These studies will have to control for many factors including method of abortion and degree of dilatation required.

MENSTRUAL REGULATION

Menstrual regulation (MR) is a procedure used to terminate a suspected pregnancy within 14 days after the expected onset of a menstrual period (164). The concept was a natural extension of the desire to reduce complication rates which increase with gestation. But MR is complicated by the lack of a readily available test that can determine pregnancy within two weeks of expected onset of menses.

In the past, there has been widespread use of hormones as a test for pregnancy. It was assumed that if menstruation did not follow a short course of progesterone or combined estrogen/progesterone that the patient must indeed be pregnant. The FDA has prohibited this use on the basis that these hormones could cause congenital malformations if the pregnancy continued to term. It has also been recently shown, as seen in Figure 28, that these hormones actually delay the onset of menstruation of nonpregnant women, besides causing mild side effects such as nausea (165).

The most commonly used procedure for menstrual regulation is vacuum aspiration using a 4 to 6 mm flexible plastic cannula and a modified 50 cc syringe (Gynecologic Kit, International Pregnancy Advisory Services, Chapel Hill, NC, USA) as a source of vacuum (Figure 29). The cannulae can generally pass the internal os without anesthesia. A paracervical block is sometimes given for nulligravid women. The double-cut design of Karman provides increased flexibility when the cannula meets any resistance and thus reduces the possibility of perforation. Vacuum is produced by closing the pinch-valve and withdrawing the piston to a locked position. After it is attached to the previously inserted cannula, the valve is opened. As in the case of later first trimester abortions, care must be taken to completely evacuate the uterus (166).

The primary drawback of menstrual regulation is the lack of a test that can accurately diagnose pregnancy before 6 menstrual weeks; therefore, some procedures are performed on nonpregnant women. Figure 30 shows the increasing proportion of women who are actually pregnant by day of delayed menses. Depending upon how early or late the procedure is performed, 25 to 50 percent of the women who are 1 to 14 days delayed in onset of their expected menstrual periods will

actually not be pregnant (167). These unnecessary procedures must be weighed against the rising complication rate of procedures performed later in pregnancy (Figure 31).

The characteristics of standard immunologic urinary pregnancy tests such as the Pregnosticon Dri-Dot® Test (Organon, Inc., West Orange, NJ, USA) can be examined to determine their usefulness in avoiding these unnecessary procedures. This rapid, slide test designed to detect 1.5 IU HCG per milliliter is quite accurate if the test is positive, but its false-negative rate is over 80 percent at less than 35 days from the last menstrual period, declining to 5 percent by 45 days (163). The probabilities of pregnancy in the first 14 days of a missed menstrual period when the test is positive, indefinite, and negative are shown in Figure 32.

One model suggested is to delay the menstrual regulation procedure for one week for every patient with a negative pregnancy test (169). In order to determine if this will reduce complications among any group of 100 women requesting menstrual regulation, it is necessary to determine their complications when the procedure is performed on the day they present themselves between 1 and 14 days delayed menses and the potential complications to the group if the women with a negative test are re-examined in one week. Some of these women will spontaneously menstruate in the one week interval and avoid the procedure altogether; the remaining will receive the procedure at an increased risk due to the rising complication rate with time. Figure 33 shows the actual and projected complication rates by days delayed menses for the two cohorts of women. The total complication rate for the two groups is 3.9 per 100 women when the procedure is performed on the first visit and 3.7 when it is delayed one week for women with

negative pregnancy tests on their first visits (170). The savings in complications is marginal and one must conclude that readily available pregnancy tests offer little assistance in the decision of when to perform menstrual regulation. Pregnancy tests are helpful at a one-week follow-up visit when, if positive, they will alert the physician to a failed procedure, which occurs in about 1 percent of the cases, or to a possible ectopic pregnancy.

When improved pregnancy tests, such as radioimmunoassays and radioreceptor assays become generally available, this dilemma may disappear. However, by then there may be inexpensive, safe and effective pharmacologic methods of menstrual regulation that may be self administered. The usefulness of pregnancy tests would then have to be re-evaluated.

Reports by Bygdeman et al. (171) of self-administered vaginal suppositories of 15(S)-15 methyl prostaglandin $F_{2\alpha}$ methyl ester for menstrual regulation have been encouraging, although others have failed to repeat their results. Among 16 patients treated, including six who were not pregnant, all 10 pregnancies were terminated. The average duration of bleeding for those who were not pregnant was 6.5 days and for pregnant patients about 8 days. None of the patients experienced heavy bleeding requiring curettage. The patients described the bleeding as similar to a normal menstrual period.

Further improvements in pharmacological methods of menstrual regulation can certainly be expected, and they will drastically change present patterns of contraceptive practice.

TITLES AND LEGENDS

Fig. 1 Title: Demand for the principal fertility control modalities.

Legend: From: Bloch, L S (Ed.): Population Change: A Strategy for physicians. Proceedings of the International Conference on the Physician and Population Change, Stockholm, Sweden, Sept. 4, 1974. Association of American Medical Colleges, Washington, D.C.

Fig. 2 Title: The Lippes Loop IUD.

Legend: None

Fig. 3 Title: The Copper-T and Copper-7 IUDs.

Legend: None

Fig. 4 Title: The Progestasert IUD.

Legend: None

Fig. 5 Title: Two-year pregnancy and bleeding/pain removal rates for selected IUDs as a function of their surface areas.

Legend: None

Fig. 6 Title: The Spring Coil and U-coil IUDs.

Legend: None

Fig. 7 Title: Bleeding/pain removal rates by month post-insertion among 250 copper and 200 AMCA U-coil acceptors.

Legend: From: Ragab, M I & Thomas, M N (70).

Fig. 8 Title: Menstrual blood loss among women using inert and progesterone-releasing U-coils.

Legend: From: Hefnawi, et al. (71).

Fig. 9 Title: Modified Lippes Loop IUD with silastic tines to improve postpartum retention.

Legend: None

Fig. 10 Title: Modified postpartum Lippes Loop with chromic sutures.

Legend: None

Fig. 11 Title: Percentage of women reporting intermenstrual vaginal bleeding on various days of the fourth contraceptive cycle by contraceptive and nature of crossover.

Legend: From: Ravenholt, et al. Adv Plann Parent (in press).

Fig. 12 **Title:** The mini-lap Falope Ring applicator.

Legend: Photograph courtesy of the Association for Voluntary Sterilization, New York, New York, USA.

Fig. 13 **Title:** Mini-lap kit.

Legend: (Manufactured by the International Pregnancy Advisory Services, Chapel Hill, North Carolina, USA.)

Fig. 14 **Title:** Basic steps in laparoscopic sterilization.

Legend: From: Hafez, E S E & Evans, T N (Eds.): Human Reproduction, Conception and Contraception, p. 395. Harper, New York, 1973.

Fig. 15 **Title:** Low voltage Fallopian tube coagulator and transector.

Legend: (Model 138 Cautery, manufactured by Waters Instruments, Inc., Rochester, Minnesota, USA.)

Fig. 16 **Title:** The Spring-loaded Clip.

Legend: (Manufactured by the International Pregnancy Advisory Service Chapel Hill, North Carolina, USA.)

Fig. 17 **Title:** A tubal ring.

Legend: (Manufactured by KLI, Newtown, Pennsylvania, USA.)

Fig. 18 **Title:** Spring-loaded clip operating laparoscope.

Legend: (Optic Unit manufactured by Richard Wolfe Medical Instruments Corp., Rosemont, Illinois, USA; spring-loaded clip manufactured by KLI, Newtown, Pennsylvania, USA.)

Fig. 19 **Title:** Tubal ring operating laparoscope

Legend: (Manufactured by KLI, Newtown, Pennsylvania, USA.)

Fig. 20 **Title:** Tubal ring occlusion of the Fallopian tube.

Legend: None

Fig. 21 **Title:** Comparison of 12-month life table pregnancy rates per 100 women sterilized by laparoscopy and minilaparotomy.

Legend: From: McCann, M F (115).

Fig. 22 **Title:** The Bleier Clip.

Legend: (Manufactured by Gerhard Hug GMBH, Umkirch, West Germany).

Fig. 23 **Title:** The 2.7 mm diameter laparoscope.

Legend: (The Dyonics Needlescope, manufactured by Dyonics, Inc., Woburn, Massachusetts, USA.)

Fig. 24 Title: Blind transcervical delivery system for methyl 2-cyanoacrylate (MCA).

Legend: None

Fig. 25 Title: Comparison of complication rates for menstrual regulation and pregnancy termination procedures by menstrual weeks' gestation.

Legend: From: Edelman, D A, et al: Am J Obstet Gynecol 119:473, 1974.

Fig. 26 Title: Comparison of cumulative abortion rates for intraamniotic saline and two prostaglandin $F_{2\alpha}$ dosage schedules.

Legend: From: Edelman, D A, et al: Am J Obstet Gynecol 125:188, 1976.

Fig. 27 Title: Relative risks of major morbidity with curettage, saline instillation, and $PGF_{2\alpha}$ instillation by menstrual weeks' gestation.

Legend: None

Fig. 28 Title: Percent of women menstruating within 7 days of the initial clinic visit.

Legend: The "treatment group" was given 1 mg of an estrogen-progestin combination; the control group received no hormonal injection. From: Vengadasalam, et al. (165).

Fig. 29 Title: The 50 cc syringe and 4, 5, and 6 mm plastic cannulae used in menstrual regulation procedures.

Legend: (Manufactured by the International Pregnancy Advisory Services Chapel Hill, North Carolina, USA.)

Fig. 30 Title: Prevalence of documented pregnancy by duration of amenorrhea.

Legend: None

Fig. 31 Title: Probability of unnecessary procedures and complaints/complications by duration of amenorrhea.

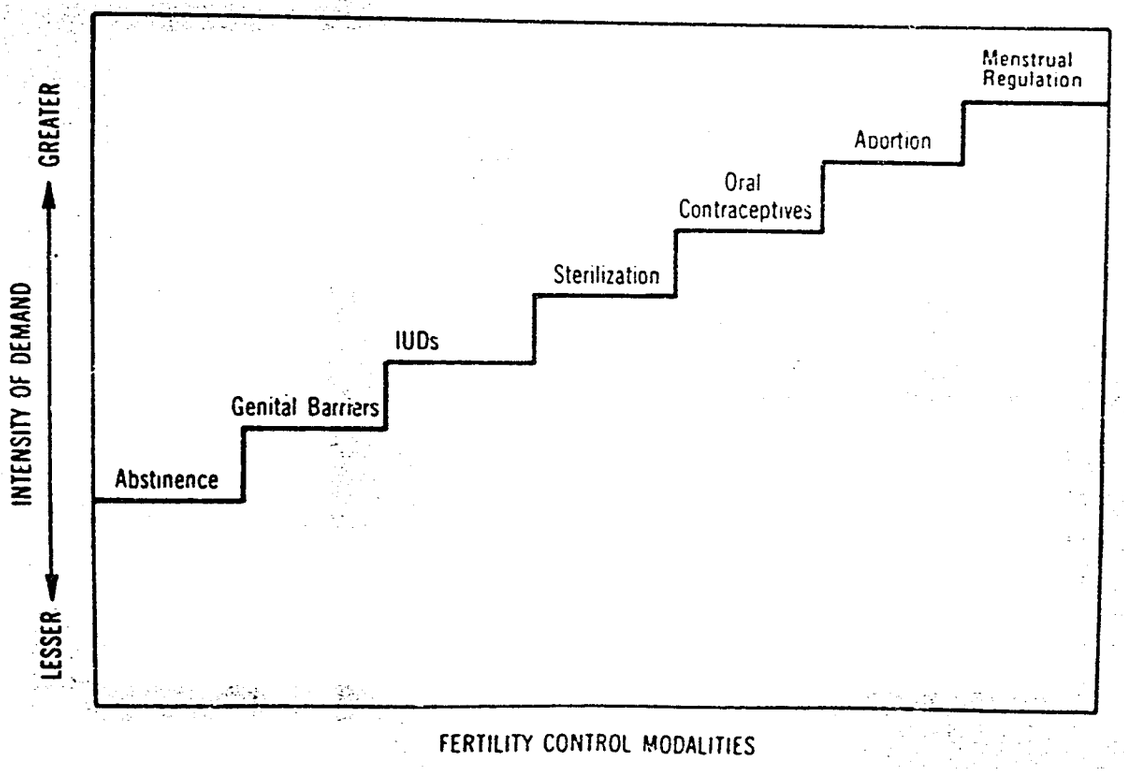
Legend: None

Fig. 32 Title: Probability of pregnancy by days' delayed menses and result of initial pregnancy test.

Legend: None

Fig. 33 Title: Comparison of complication rates for menstrual regulation performed at the initial visit and delayed for one week.

Legend: None


INTENSITY OF DEMAND
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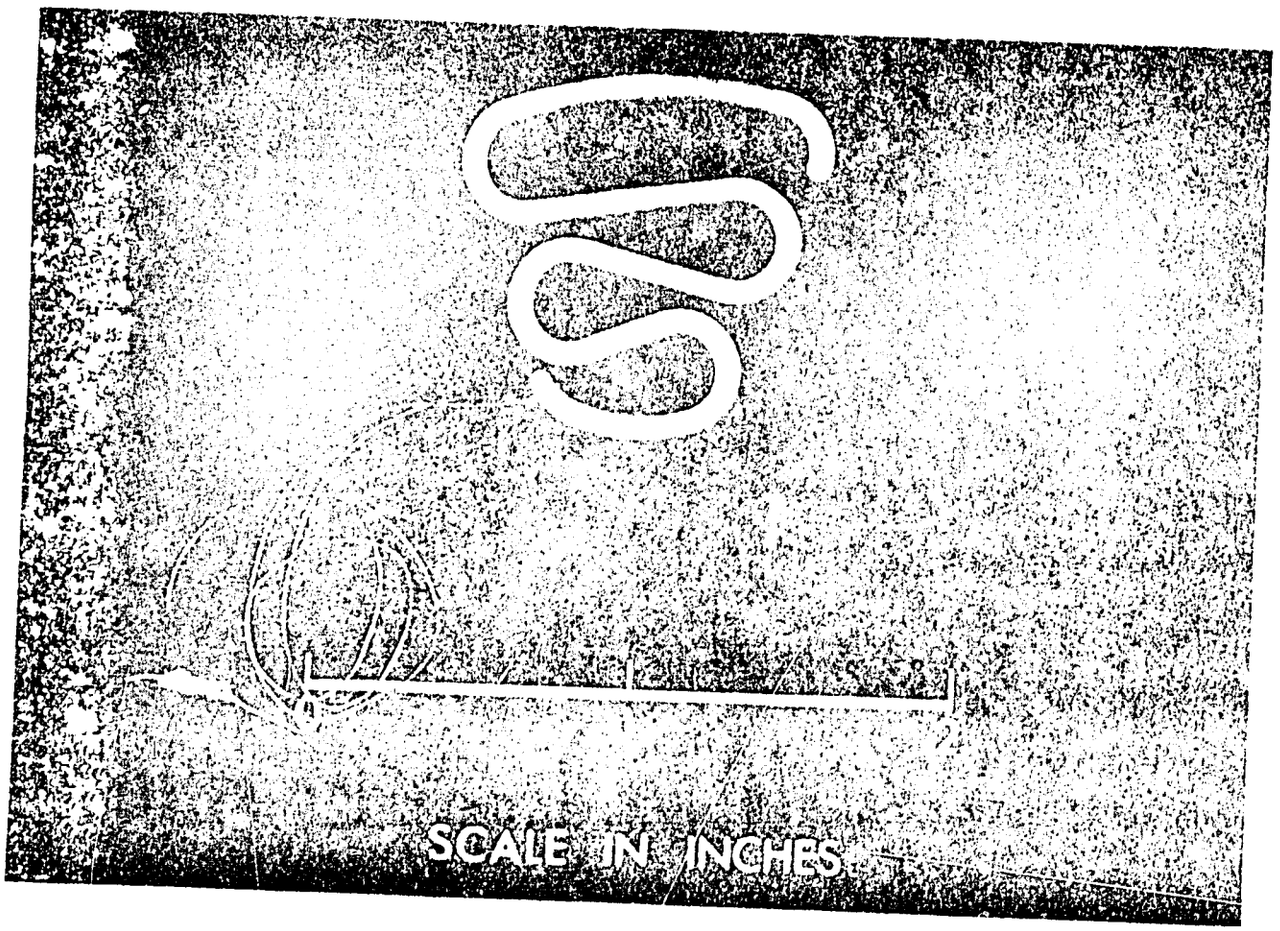
Genital Barriers
IUDs
Sterilization
Oral Contraceptives
Abortion
Menstrual Regulation
FERTILITY CONTROL MODALITIES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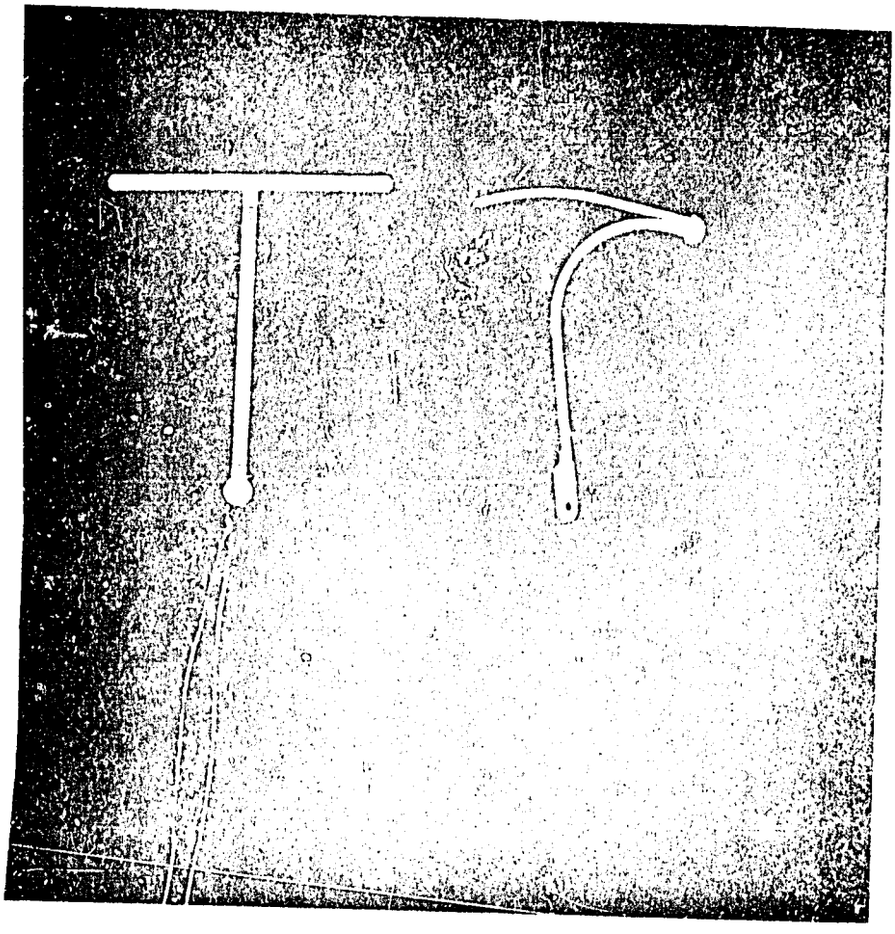

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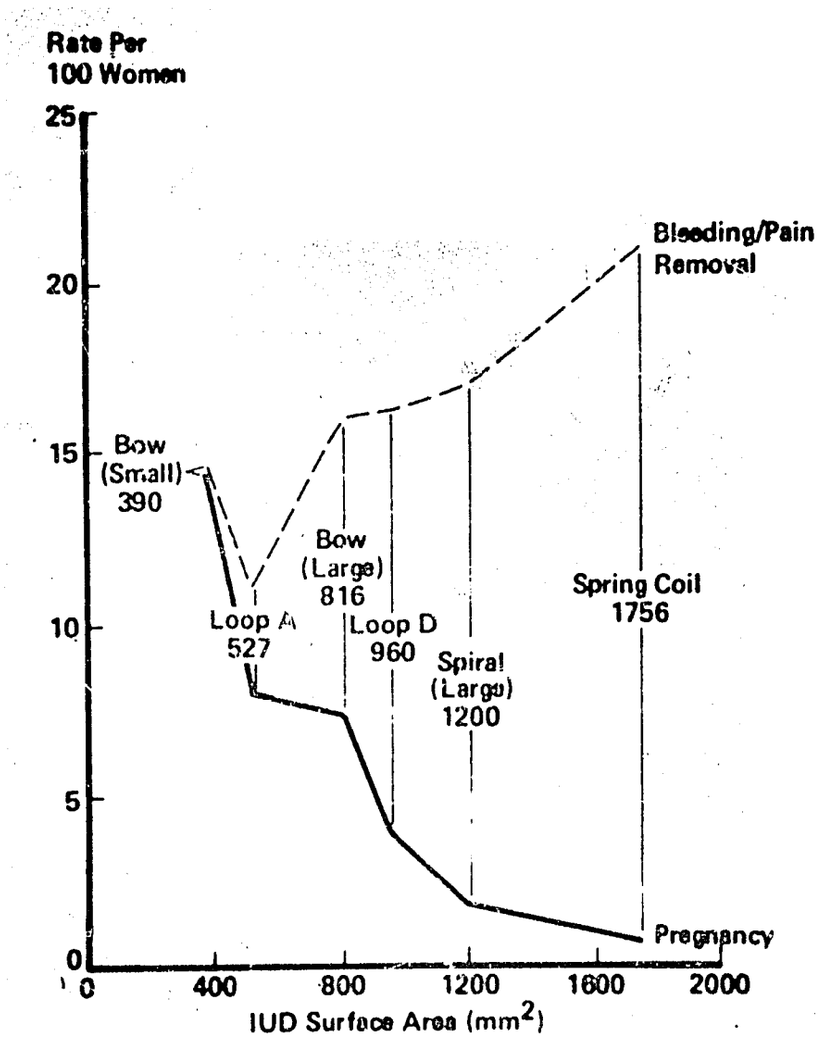
Rate Per
100 Women
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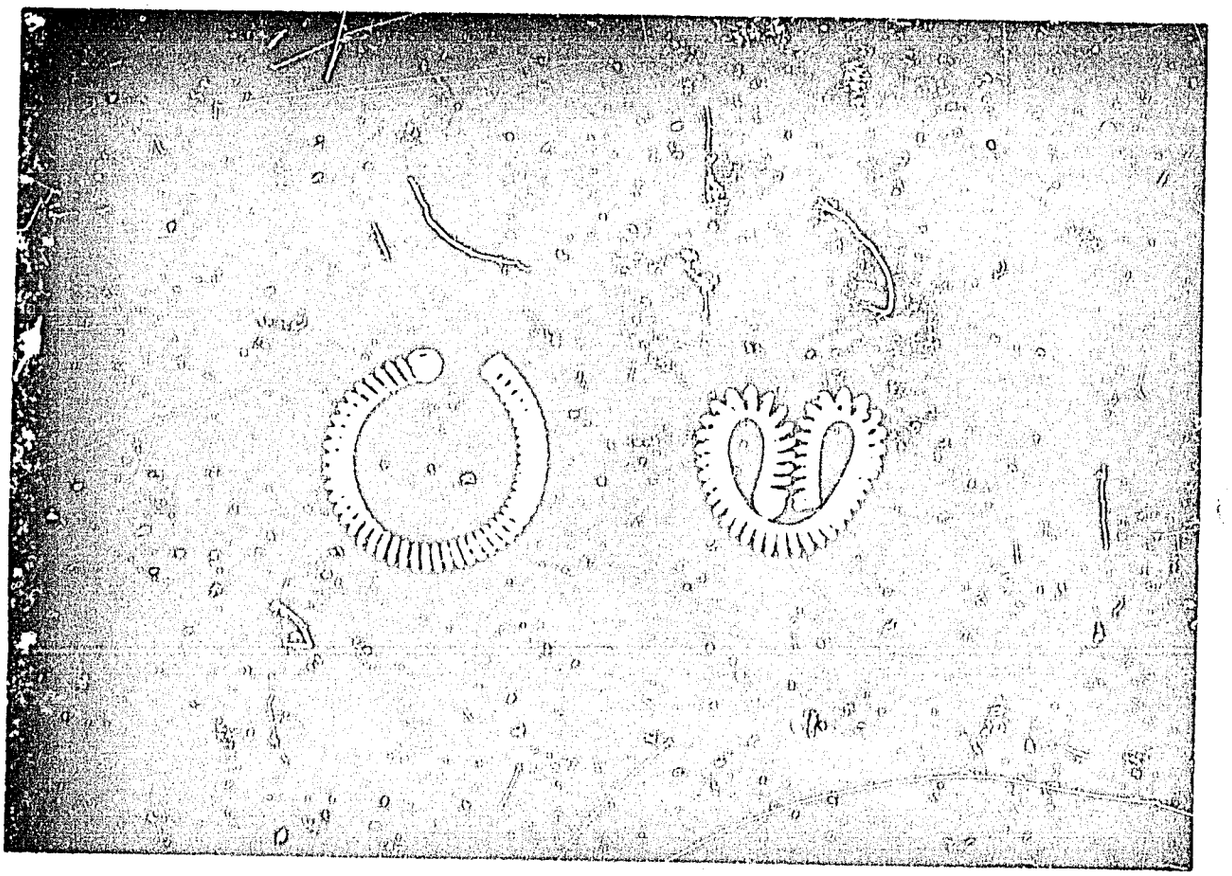
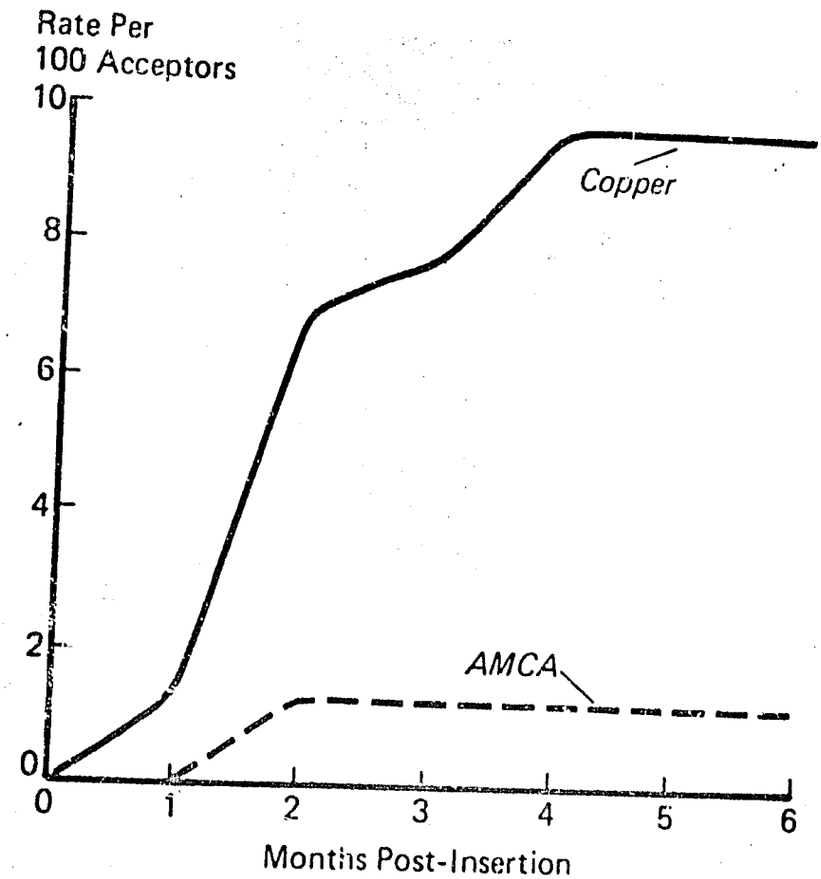
20
15
10
5
0
Bleeding/Pain
Removal
Bow
(Small)
390
Bow
(Large)
816
Loop A
527
Loop D
960
Spiral
(Large)
1200
Spring Coil
1756
Pregnancy
0
400
800
1200
1600
2000
IUD Surface Area (mm2)




Rate Per
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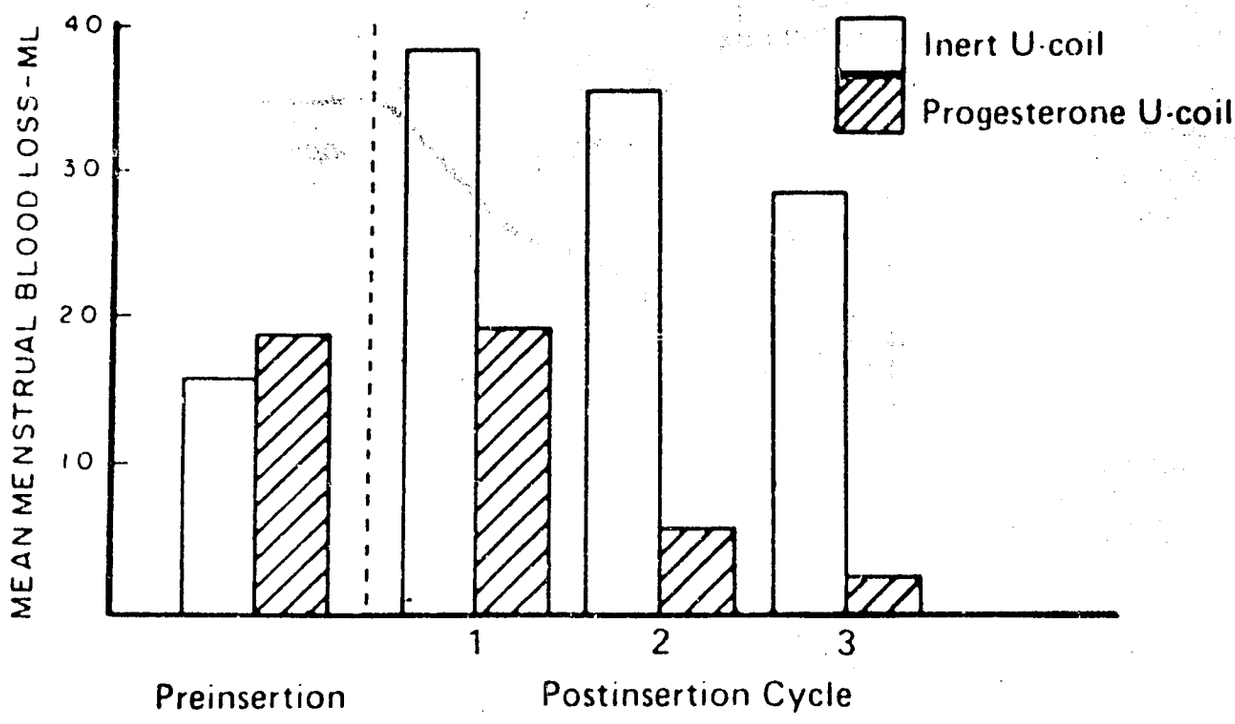
Months Post-Insertion


MEAN MENSTRUAL BLOOD LOSS - ML
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30
20
10
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Progesterone U-coil
1
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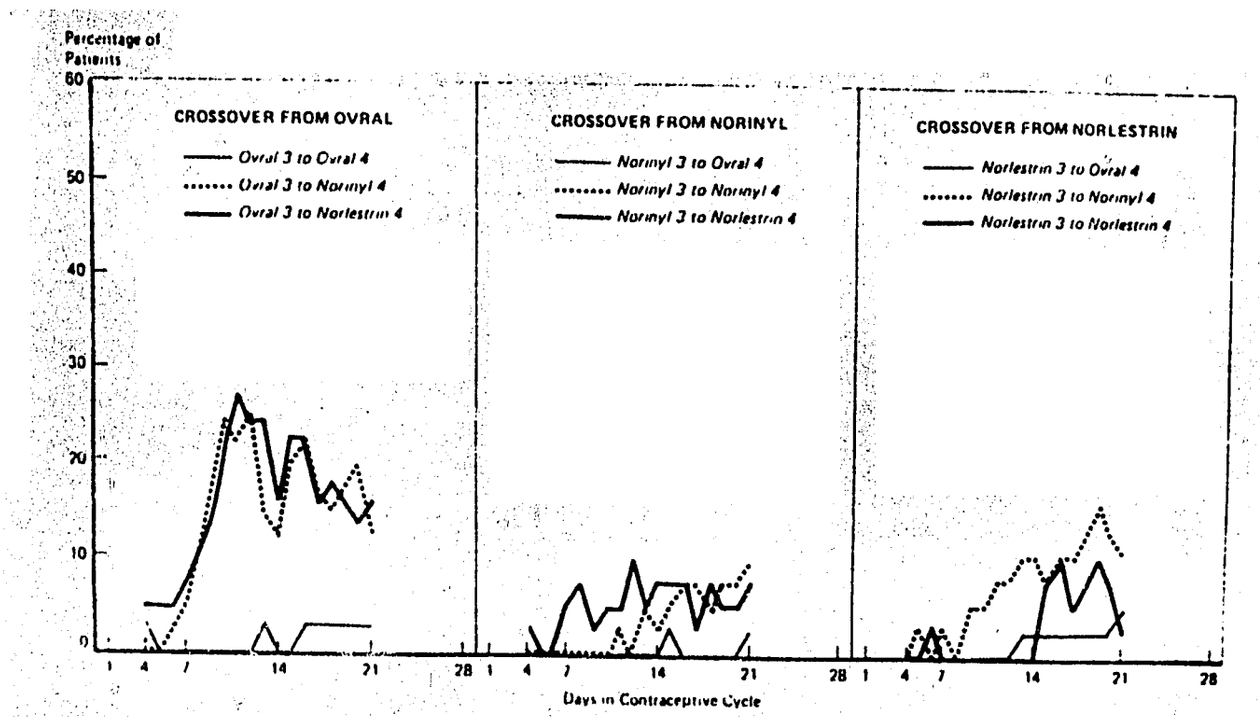
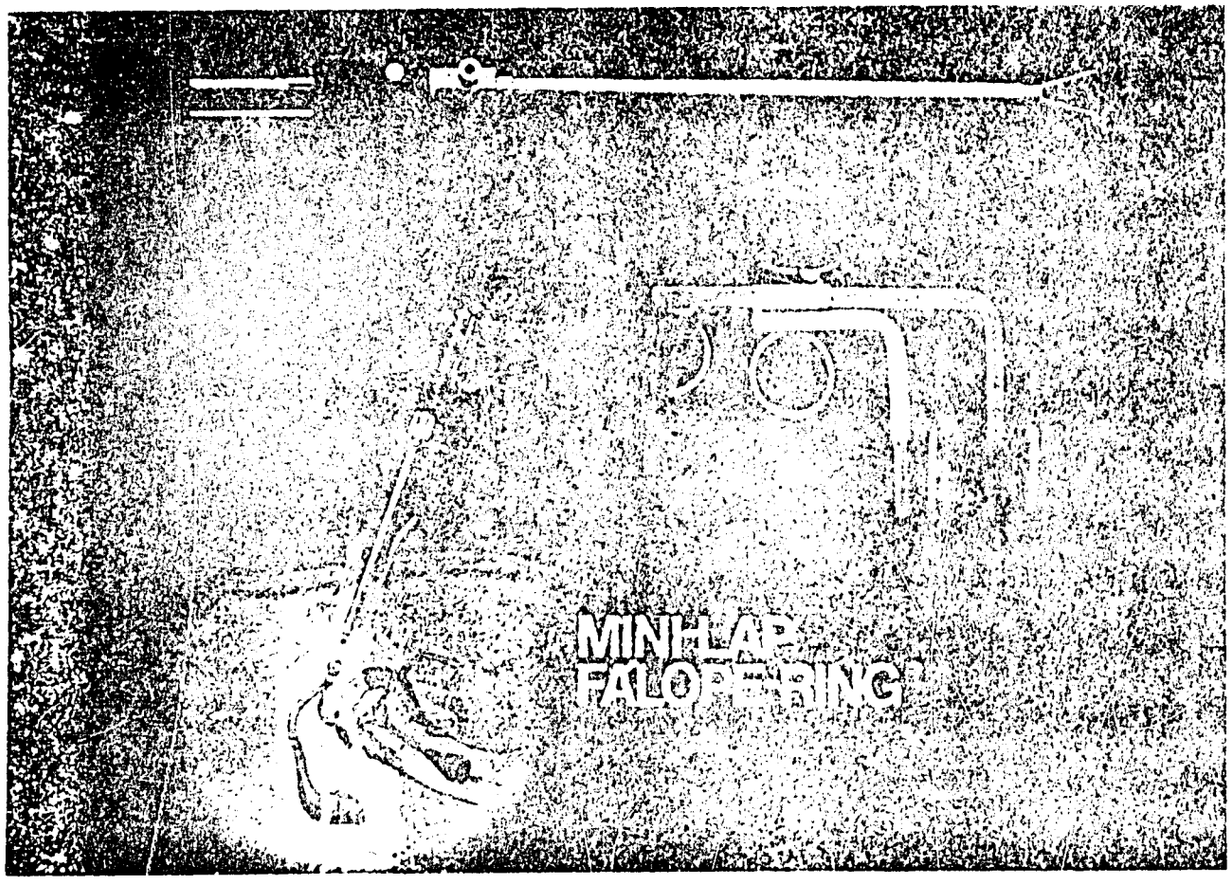
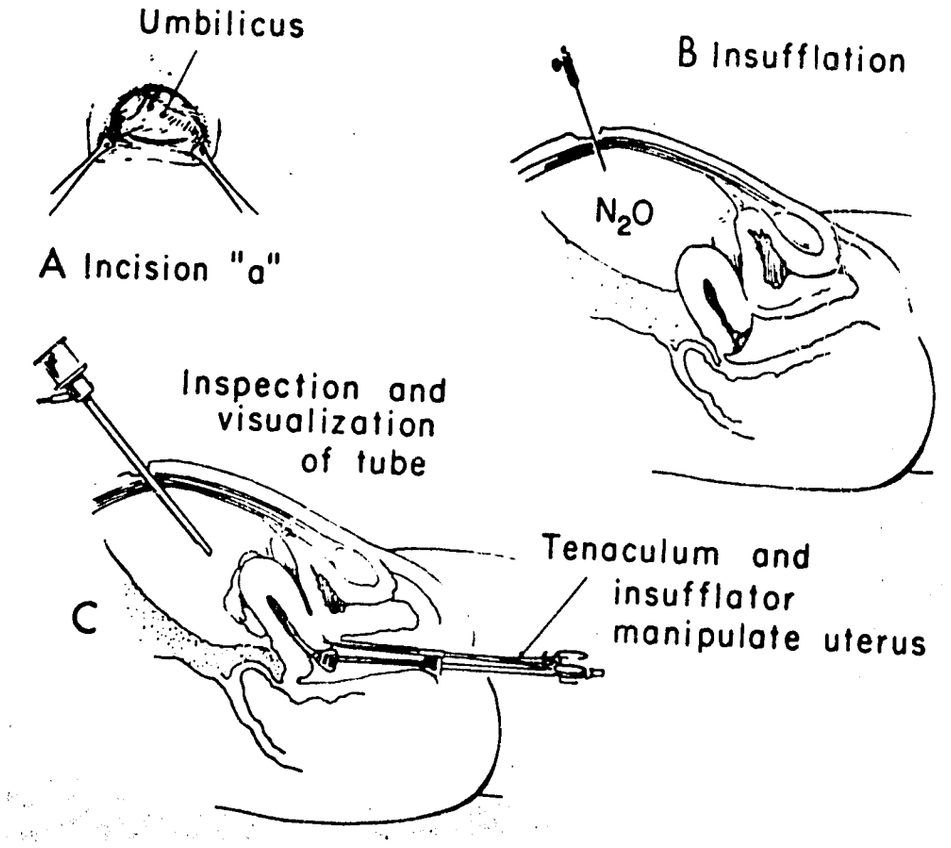
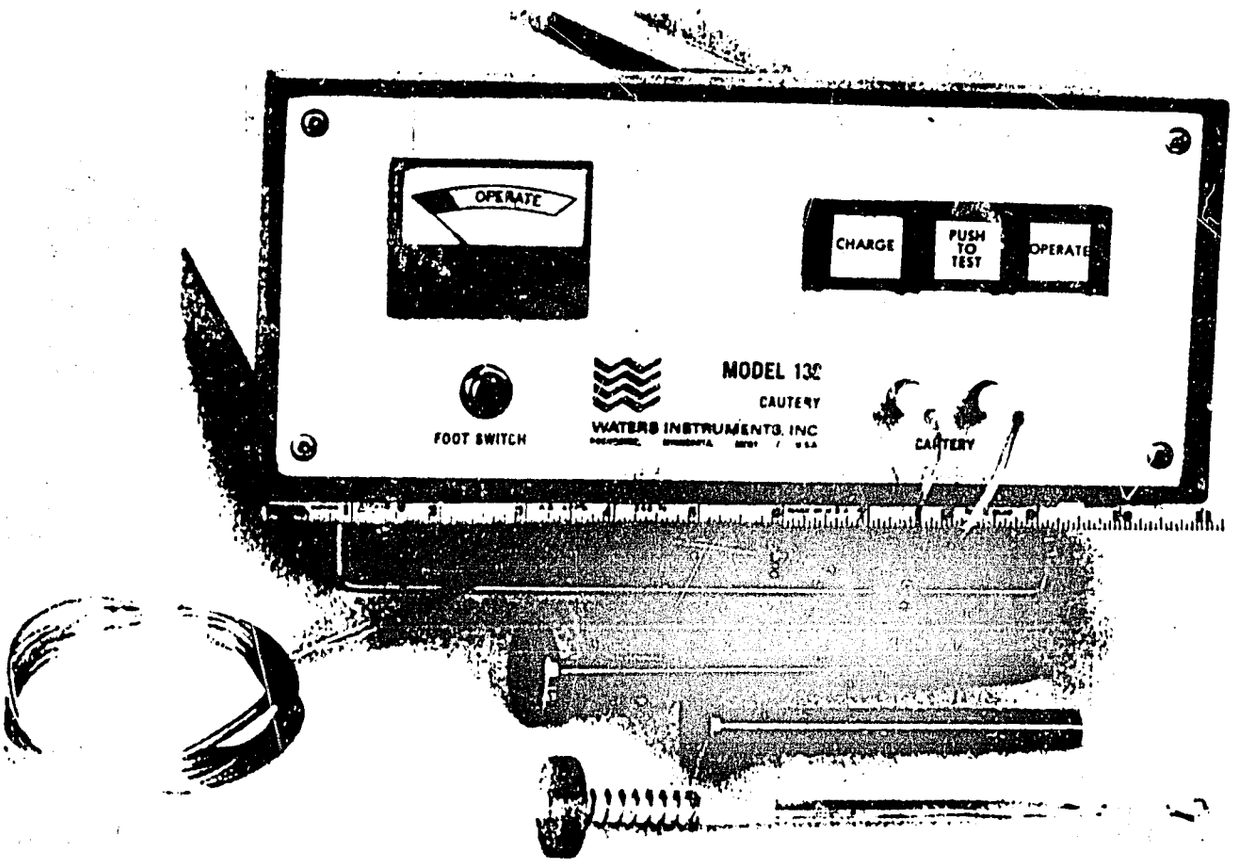
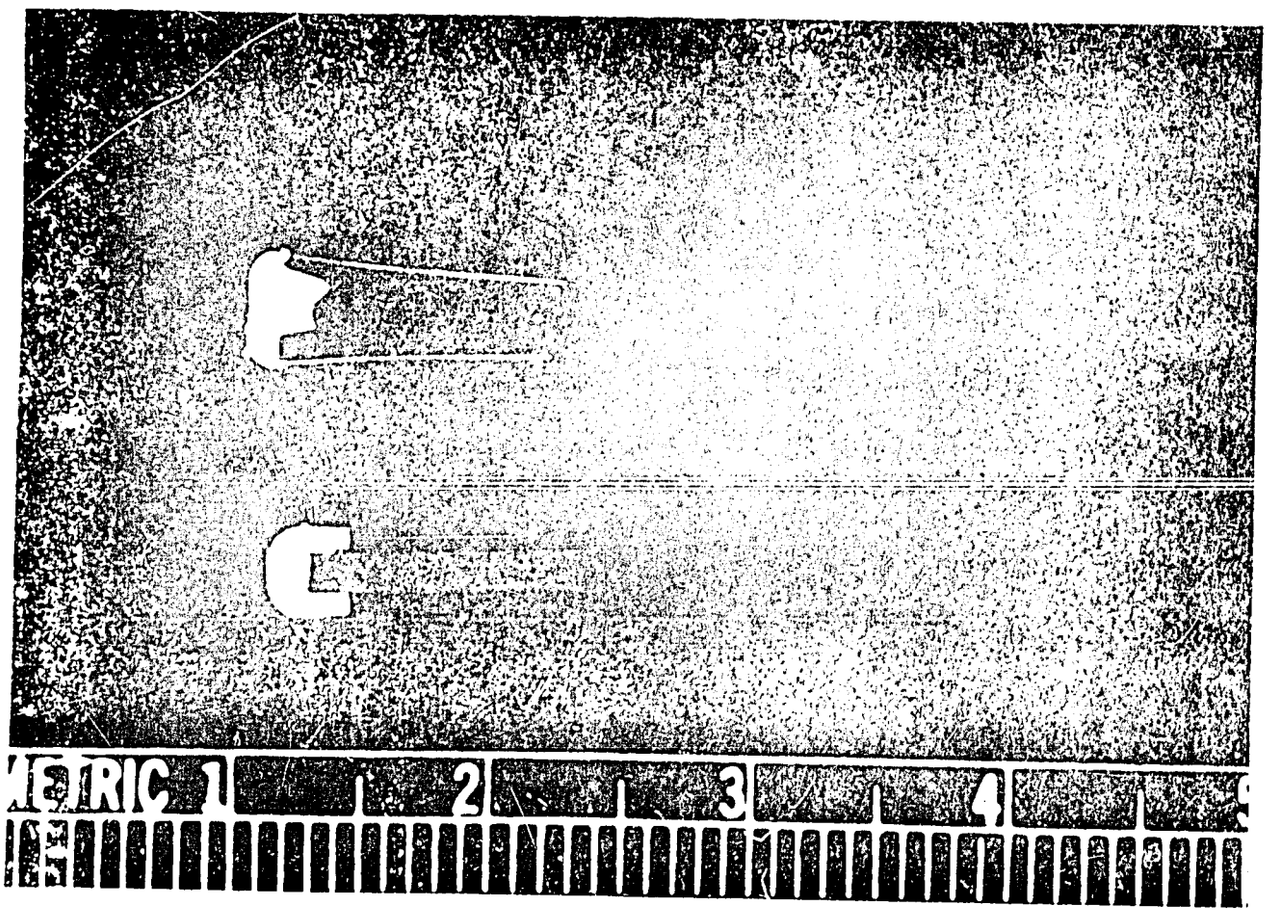
3
Preinsertion
Postinsertion Cycle

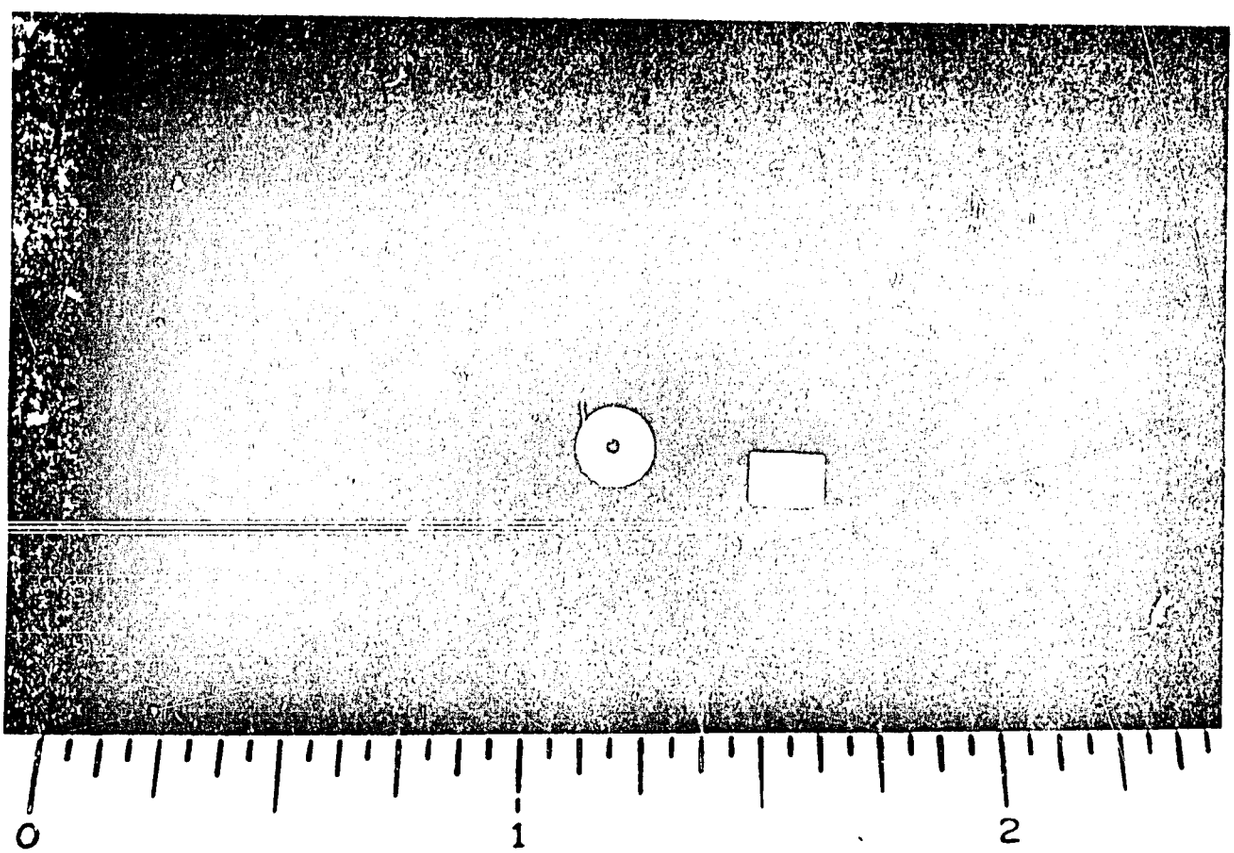

Percentage of Patients
60
50
40
30
20
10
0
CROSSOVER FROM OVRAL
Ovral 3 to Ovral 4
Ovral 3 to Norinyl 4
Ovral 3 to Norlestrin 4
CROSSOVER FROM NORINYL
Norinyl 3 to Ovral 4
Norinyl 3 to Norinyl 4
Norinyl 3 to Norlestrin 4
CROSSOVER FROM NORLESTRIN
Norlestrin 3 to Ovral 4
Norlestrin 3 to Norinyl 4
Norlestrin 3 to Norlestrin 4
1 4 7 14 21 28 1 4 7 14 21 28 1 4 7 14 21 28
Days in Contraceptive Cycle


MINELAB
FALO ENGINEERING

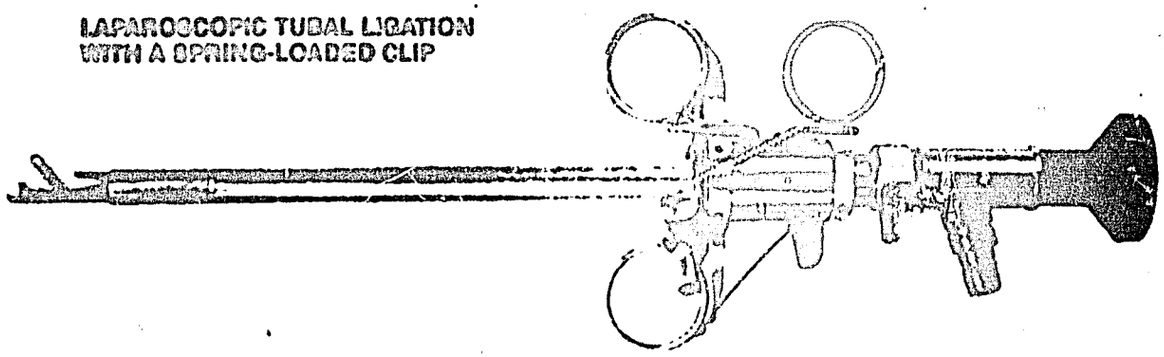

Umbilicus
A Incision "a"
B Insufflation
N_2O
Inspection and visualization of tube
C
Tenaculum and insufflator manipulate uterus

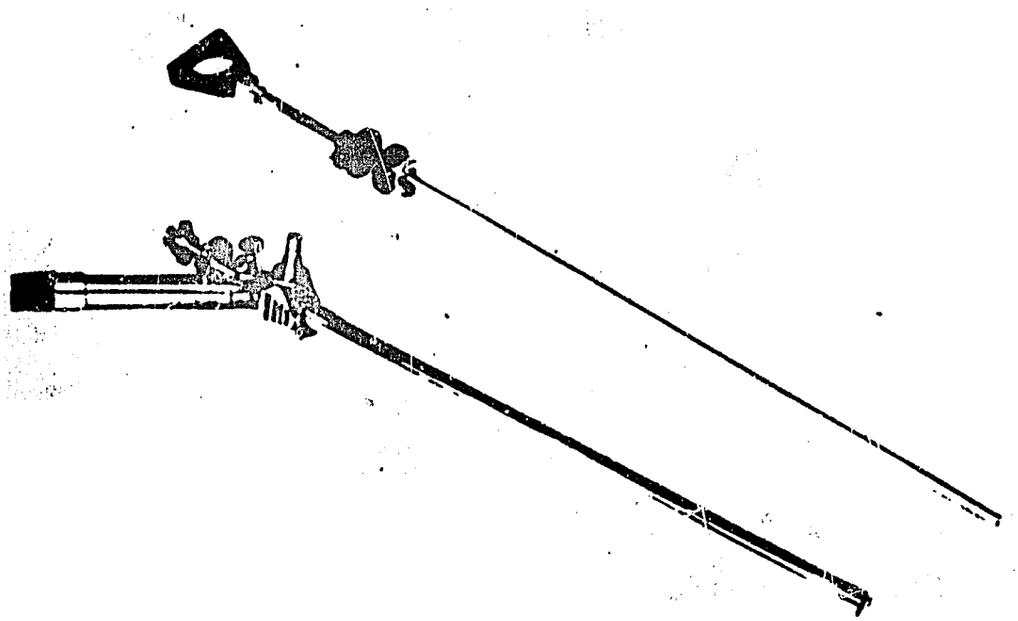

OPERATE
CHARGE
PUSH TO TEST
OPERATE
MODEL 13
CAUTERY
WATERS INSTRUMENTS, INC
FOOT SWITCH
CAUTERY

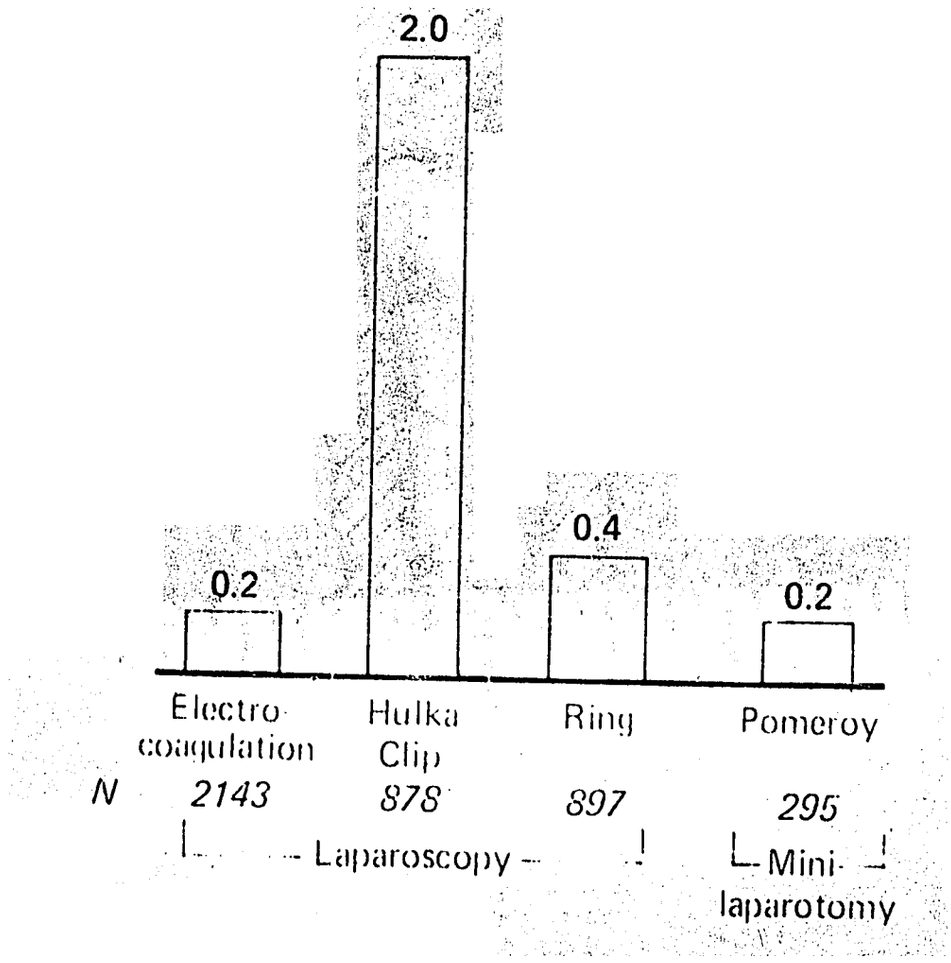

METRIC
1
2
3
4

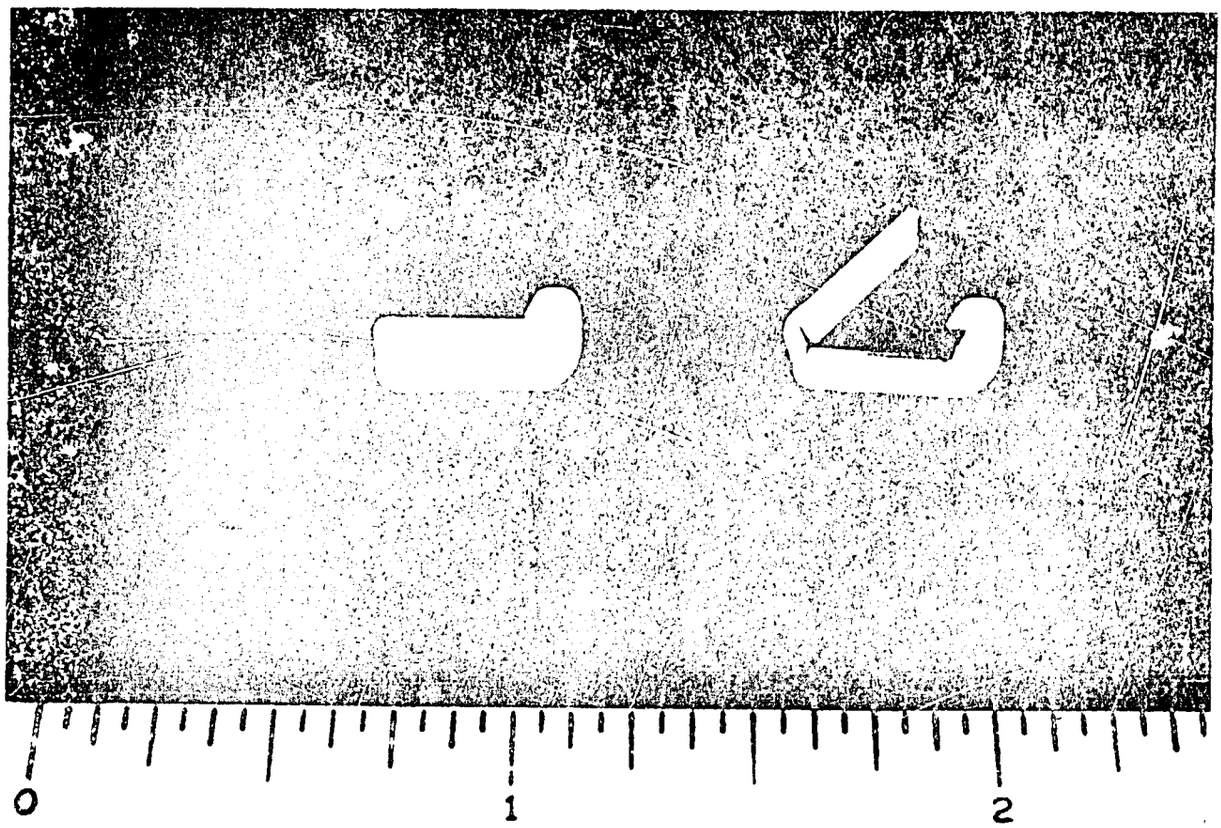

0
1
2

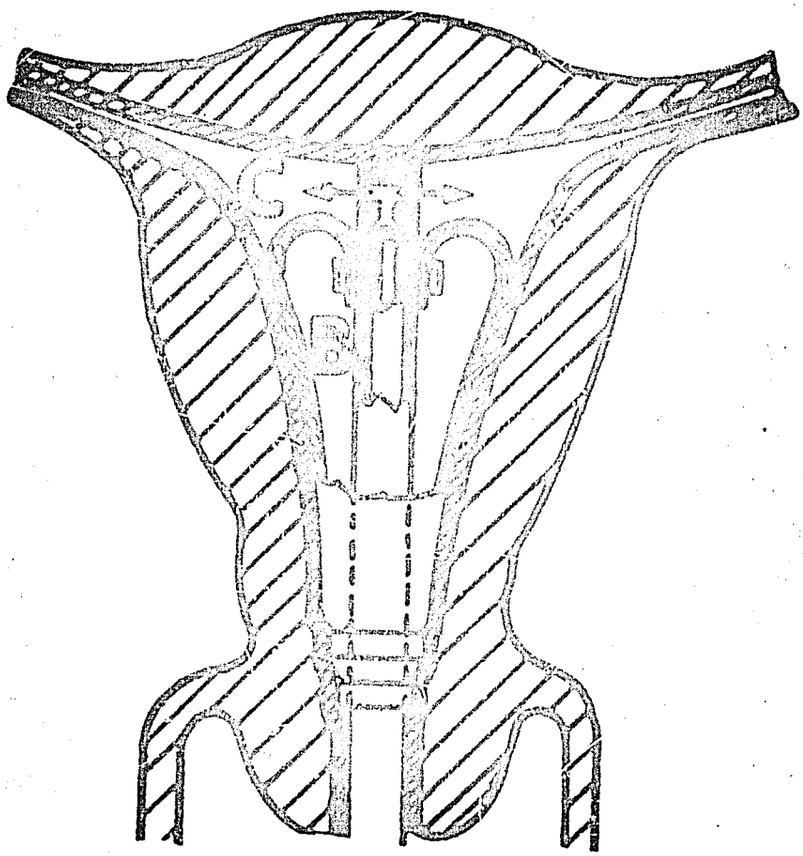
LAPAROSCOPIC TUBAL LIGATION
WITH A SPRING-LOADED CLIP

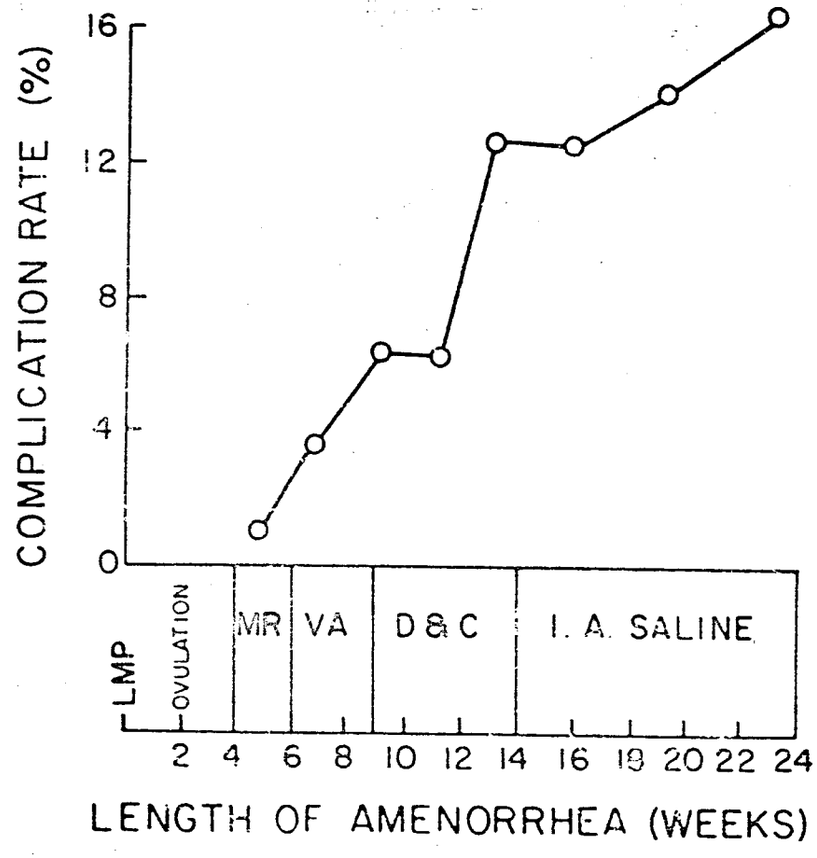


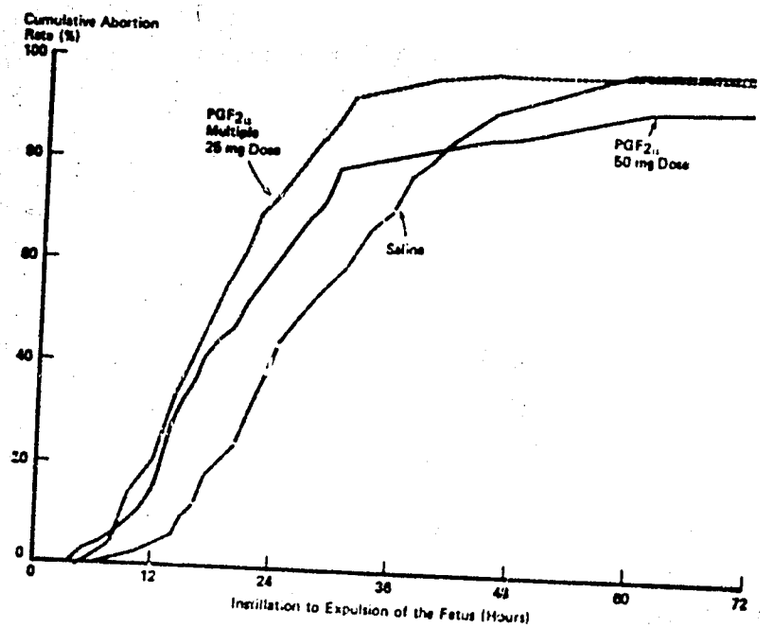



2.0
0.2
0.4
0.2
Electro-
coagulation
Hulka
Clip
Ring
Pomeroy
N
2143
878
897
295
Laparoscopy
Mini-
laparotomy

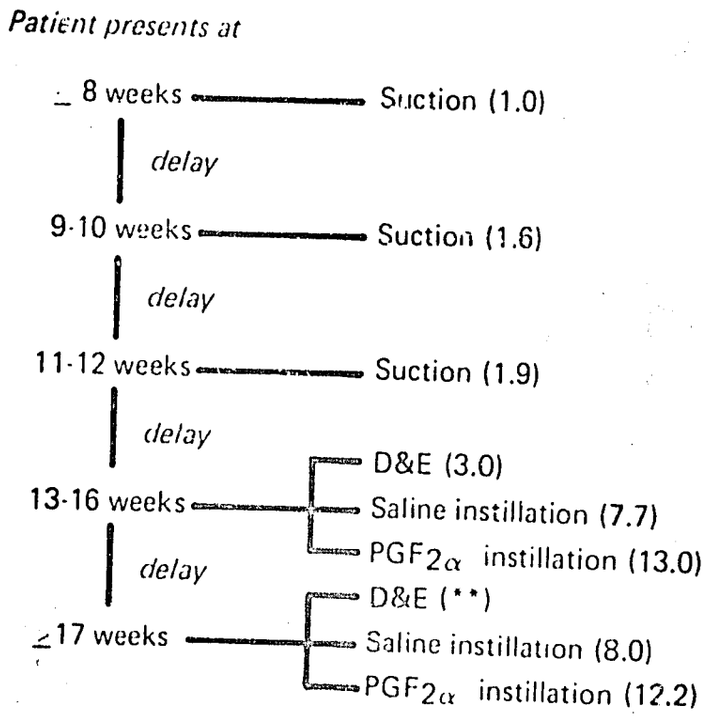

0
1
2



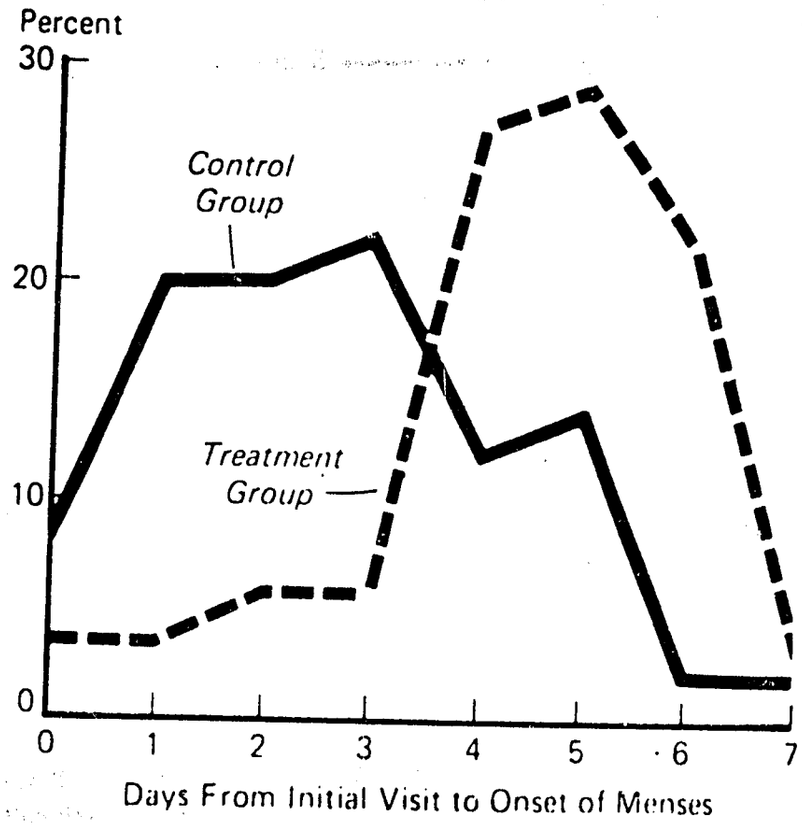

COMPLICATION RATE (%)
16
12
8
4
0
LMP
OVULATION
MR
VA
D & C
I. A. SALINE
2 4 6 8 10 12 14 16 18 20 22 24
LENGTH OF AMENORRHEA (WEEKS)

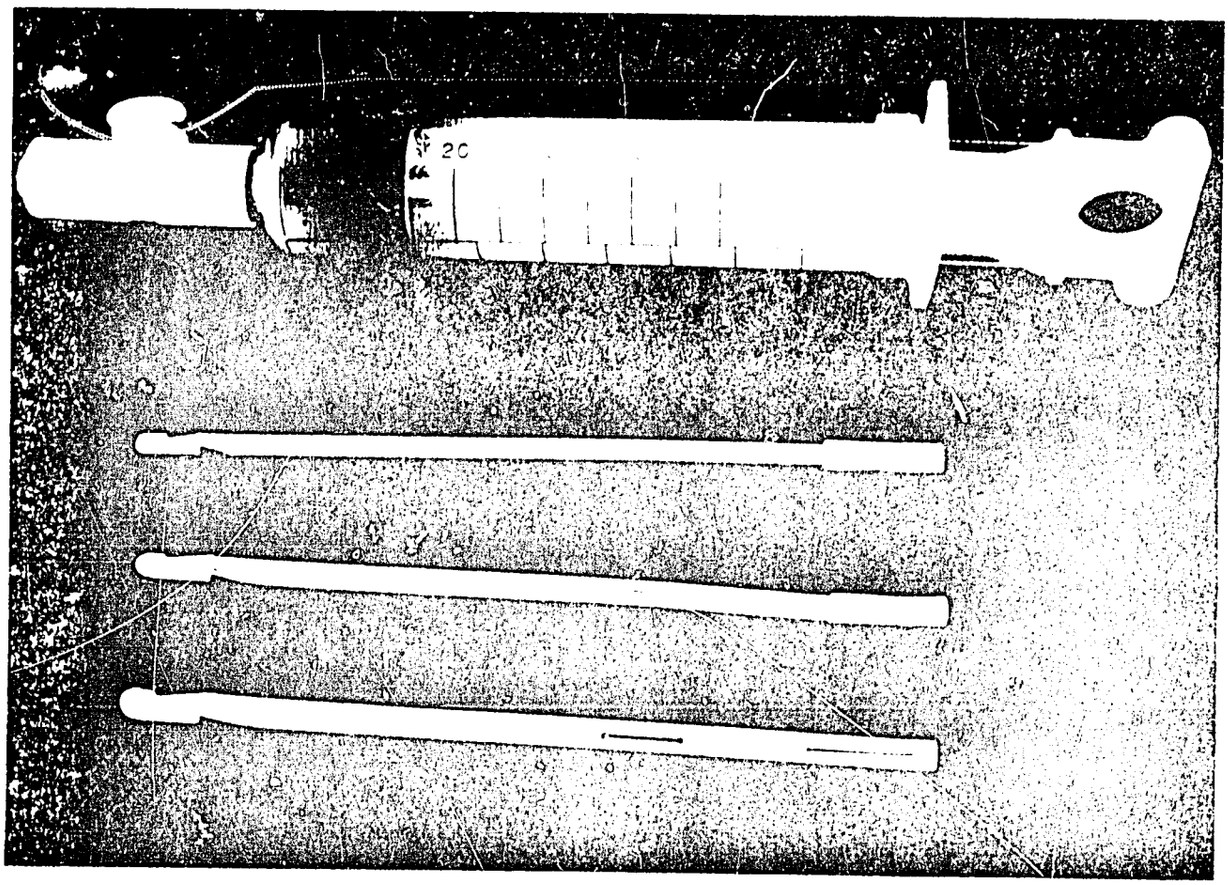

Cumulative Abortion Rate (%)
100
80
60
40
20
0
PGF2α Multiple 25 mg Dose
PGF2α 50 mg Dose
Saline
0
12
24
36
48
60
72
Instillation to Expulsion of the Fetus (Hours)

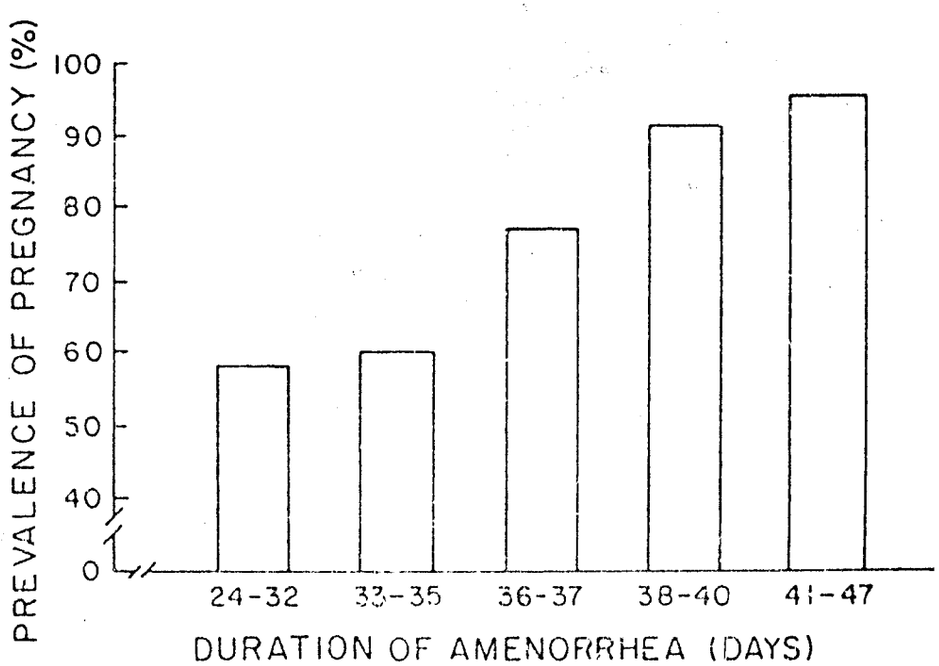
SCHEMATIC VIEW OF RELATIVE RISKS* OF MAJOR MORBIDITY

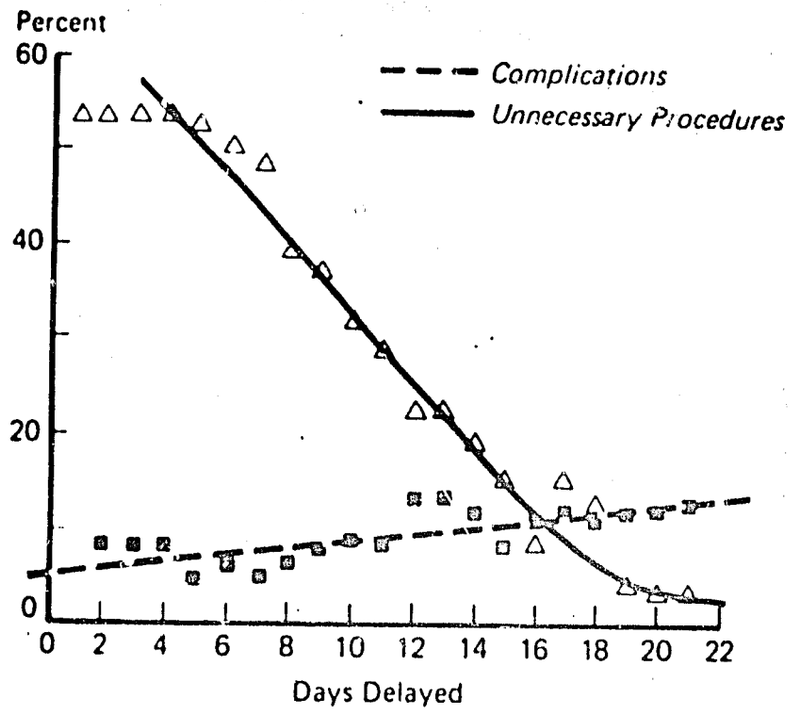


* *Ratio of rates based on index rate for suction at ≤8 weeks.*
** *Cell with ≤5 morbid cases, insufficient for valid comparison.*


Percent
30
20
10
0
Control Group
Treatment Group
0
1
2
3
4
5
6
7
Days From Initial Visit to Onset of Menses


20


PREVALENCE OF PREGNANCY (%)
100
90
80
70
60
50
40
0
24-32
33-35
36-37
38-40
41-47
DURATION OF AMENORRHEA (DAYS)


Percent
60
40
20
0
Complications
Unnecessary Procedures
0 2 4 6 8 10 12 14 16 18 20 22
Days Delayed

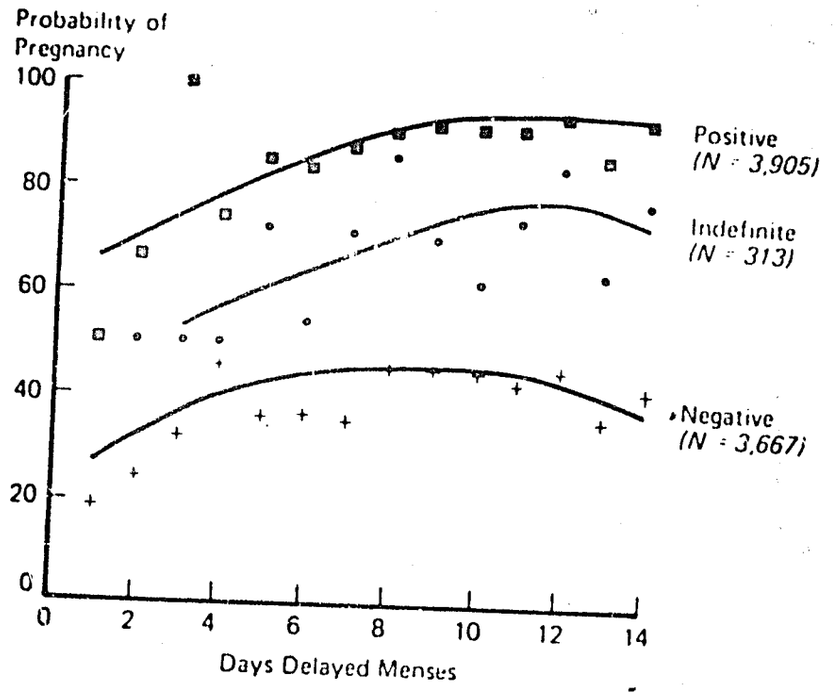
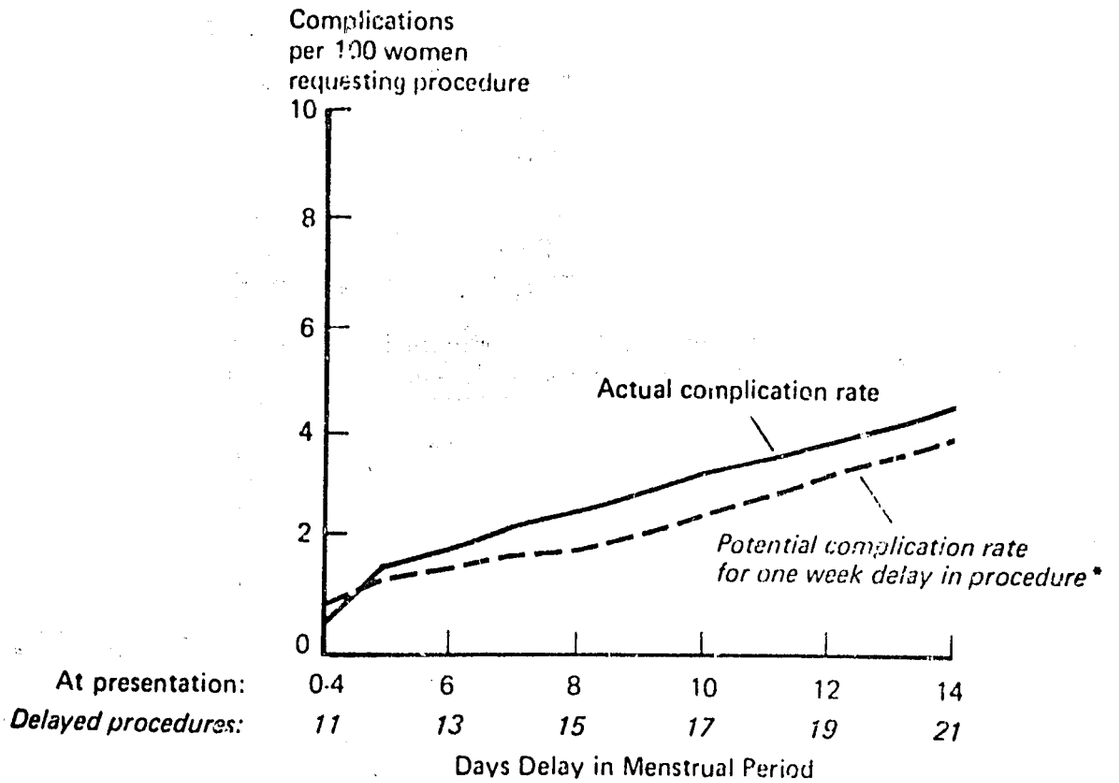


Figure 2. Probability of Pregnancy by Days Delayed Menses and by Result of Pregnancy Test


Complications
per 100 women
requesting procedure
10
8
6
4
2
0
Actual complication rate
Potential complication rate
for one week delay in procedure*
At presentation:
0-4
6
8
10
12
14
Delayed procedures:
11
13
15
17
19
21
Days Delay in Menstrual Period

NET EXPULSION RATES FOR IMMEDIATE POSTPARTUM INSERTION

Months After Insertion	Rate Per 100 Women		
	LEM	Modified Loop	Lippes Loop D
1	1.5	1.9	5.0
2	7.8	3.9	11.0
3	10.1	9.1	

ESTIMATED WORLD USE OF MEANS OF FERTILITY CONTROL
(Millions of Coupies)

	1970	1976
Sterilization	20	75
Oral contraceptives	30	55
Condoms	25	30
Intrauterine devices	12	15
Other methods*	60	65
Abortion**	30	35

* *Diaphragm, spermicides, rhythm, withdrawal, etc.*
** *Annual incidence.*

PREVALENCE OF SURGICAL COMPLICATIONS, FAILED PROCEDURES, AND READMISSIONS

Procedure	Women With 1+ Surgical Complications		Failed Procedures		Hospital Readmission	
	No.	%	No.	%	No.	%
Laparoscopy Electrocoagulation *(N = 8425)*	172	2.0	61	0.7	11	0.1
Hulka clip *(N = 1445)*	13	0.9	16	1.1	6	0.4
Rocket clip *(N = 484)*	18	3.7	1	0.2	1	0.2
Tubal ring *(N = 2904)*	82	2.8	17	0.6	5	0.2
Minilaparotomy Pomeroy *(N = 2585)*	36	1.4	29	1.1	10	0.4
Tubal ring *(N = 532)*	17	3.2	13	2.4	0	0.0

** Based on data from the International Fertility Research Program, Research Triangle Park, North Carolina 27709, USA.*

FEMALE STERILIZATION OPTIONS BY APPROACH, PATIENT CATEGORY, AND METHOD OF OCCLUDING TUBES

	Laparotomy: Plain	Laparotomy: Uterine Sound	Laparoscopy	Colpotomy	Culdoscopy	Hysteroscopy	Blind Transcervical
Patient category							
Interval	•	•	•	•	•	•	•
Post-delivery	•						
Postabortion							
1st trimester	•	•	•	•			
2nd trimester	•		•				
Method of occluding tubes							
Ligature	•	•		•	•		
Electrocoagulation			•			•	
Spring-loaded clips	•	•	•	•	•		
Tubal rings	•	•	•	•	•		
Chemical agents						•	•
Intraluminal plugs						•	•

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