Long-term contraception with the Levonorgestrel 20 mcg/day (LNg 20) and the Copper T 380Ag intrauterine devices: A five-year randomized study

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ABSTRACT

An intrauterine device, releasing approximately 20 µg/day of levonorgestrel (LNg 20), used by 1124 women, was studied in a randomized trial of five years duration in comparison with the Copper T, model TCu 380Ag, in 1121 women. At five years, the gross cumulative pregnancy rate of 1.1±0.5 per 100 among users of the LNg 20 devices was not significantly different from the rate of 1.4±0.4 per 100 experienced by users of the Copper T 380Ag. The steroid-releasing IUD had significantly higher termination rates for expulsion and amenorrhea, a significantly lower termination rate for other menstrual problems and pain, and a lower continuation rate. The five-year continuation rate among women using the TCu 380Ag was 40.6 per 100 as compared with that of 33.0 per 100 among women randomized to the LNg 20 device ($P<.001$). Terminations attributed to amenorrhea with the LNg device primarily account for differences in continuation.

These two intrauterine devices are the most effective long-term, reversible IUDs yet reported in the literature. No other contraceptive methods have exhibited such low long-term pregnancy rates in randomized comparative trials.

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INTRODUCTION

Truly long-term, reversible contraception of five or more years following a single application has been demonstrated in few randomized studies. The World Health Organization (WHO) has reported a randomized trial of the TCu 380A and the TCu 220C IUDs through six years of first segment use (1); in Scandinavia, Luukkainen and colleagues have published a comparative trial of the Nova T and the TCu 200Ag IUDs through five years (2). Hitherto, randomized five-year trials of a steroid-releasing method, whether implant, injectable, oral, vaginal ring, or IUD, have not been published. Steroid release rates of implants and IUDs diminish with time; rising pregnancy and ectopic pregnancy rates signal the end of their effective life. The Progestasert®, 65 µg/day device, is limited to a period of 12-18 months of use. An allied progesterone-releasing device had diminished release rates and increased pregnancy and ectopic pregnancy rates at about 30 months (3). A truly microdose levonorgestrel-releasing intrauterine device, rated at 2 µg/day, was associated with undesirably high pregnancy and ectopic pregnancy rates in comparison with the Copper T 220C IUD (4), as have low doses of other progestins used for intrauterine contraception (5).

The Population Council, holder of a patent for a levonorgestrel-releasing IUD, undertook a long-term trial of a device rated to release 20 µg/day of levonorgestrel. The study measured standard performance characteristics - pregnancy, expulsion and removal rates occasioned by medical or by personal reasons - in randomized comparison with a collared copper device, the TCu 380Ag. Data in this report pertain to five years of use.

MATERIALS AND METHODS

Devices

The levonorgestrel IUD (LNg 20) carries the steroid in a homogenous rod mixed with an equal weight of medical grade silicone rubber elastomer. The rod is covered by thin-walled Silastic® tubing and is set on the vertical polyethylene stem of the frame also employed for the Nova T IUD. Devices used in five clinics contained approximately 60 mg of levonorgestrel and had an expected life of seven years; devices used in Singapore and Los Angeles contained 46 mg of levonorgestrel, and were expected to remain effective for five years. All the levonorgestrel devices were manufactured by Leiras Pharmaceuticals, Turku, Finland, and have a nominal release rate of 20 µg/day.

The Copper T, model TCu 380Ag, has a 0.25 mm diameter wire with a surface area of 310 mm^2 wound tightly around the vertical shaft of the T. This wire has a silver core designed to prevent the fragmentation and loss of coils that occur in devices carrying copper-only wire. Collars on the horizontal bar of the T provide 70 mm^2 of additional copper surface. TCu 380Ag devices in this study were manufactured by Outokumpu Oy, Finland.

Selection and Procedures

Volunteers were fertile women, ages 18-38, without contraindication to copper IUDs or contraceptive steroids. A history of PID after the last pregnancy or a history of ectopic pregnancy precluded entry to the study because of possibly impaired fecundity.

Subjects gave informed consent to random assignment of devices and to clinic visits at 1, 3, 6 and 12 months after insertion, and semi-annually thereafter. Post termination visits were requested. Women agreed to gynecologic examinations at initiation and at semi-annual visits throughout their participation and to maintain daily menstrual records.

Design

The study envisaged inclusion of 2400 subjects, half randomly assigned to the steroid-releasing device. Annual continuation rates of the order of 75-80 per 100 were expected (6), which would yield a five-year continuation rate of approximately 30 per 100. Assuming these continuation rates, one could distinguish between a fifth year annual failure rate of 1 per 100 or less on the one hand, and a fifth year failure rate of 3 per 100 or greater with 80 percent power for each device. The study also sought to distinguish between a gross cumulative pregnancy rate of 3 per 100 or higher for one device at five years and a cumulative pregnancy rate of 1 per 100 or less for the other device with 80 percent power.

Concerns developing from the litigious atmosphere surrounding IUDs in the United States in the early and mid-1980s constrained enrollment to be 6-7 percent smaller than had been planned.

Random numbers, generated by the linear congruent algorithm, determined method assignment at each clinic. Devices and insertion tubes in sterile containers were sealed inside opaque, numbered envelopes, in accordance with the random assignment, and opened in ascending numerical order in chronological sequence of presentation immediately prior to insertion. The study was single blind. Women were not told which device they had received.

Status and Analysis

Enrollment began in 1981 and continued through 1986. At the cut-off date of 31 May 1989, the overwhelming majority of women who would ever complete five years of the study had done so. Sixteen users of the LNg 20 IUD and 22 women with the TCu 380Ag device who had not completed five years were still active at the cut-off date. Computer analysis initiated in September, 1989, allowed three months for detection and transmission of data on pregnancies and other terminations occurring immediately prior to the cut-off.

Actuarial life table analyses use the Tietze conventions, modified by Jain and Sivin (7). Women, not known to have terminated, who were last seen 7 or more calendar months before the cut-off date were considered as lost to follow-up. Data for them are carried to their last clinic visit. Throughout the text, event (termination) rates correspond to single decrement or gross rates. These rates are not additive. Additive or multiple decrement rates through five years are represented in Figures 1 and 2. At each six-month interval in Figures 1 and 2, the vertical distance between successive curves represents the cumulative rate of the decrement named there. Single or multiple decrement continuation rates are identical.

Characteristics of Subjects

Randomization within clinic allocated subjects to devices without large or statistically significant differences in characteristics. Mean age was 26.6±0.1 for the LNg 20 group and 26.7±0.1 for the Copper IUD subjects (Table I). Mean parity was 2.4±0.04 for each group. On average, admission to the study was 24 months after the last pregnancy. One-third of the subjects expressed a desire to have one or more additional children.

RESULTS

Insertion-related problems

Physicians noted difficult insertions and failed insertions significantly more frequently ($P<.05$) when inserting the LNg 20 device than when inserting the Copper device. Insertion failures represented one percent of attempts to insert the steroid-releasing device and 0.2 percent of attempts using the TCu 380Ag. Women assigned to the LNg 20 device more frequently reported moderate or severe pain at insertion than did women assigned the Copper T device ($P<.0001$) (Table II).

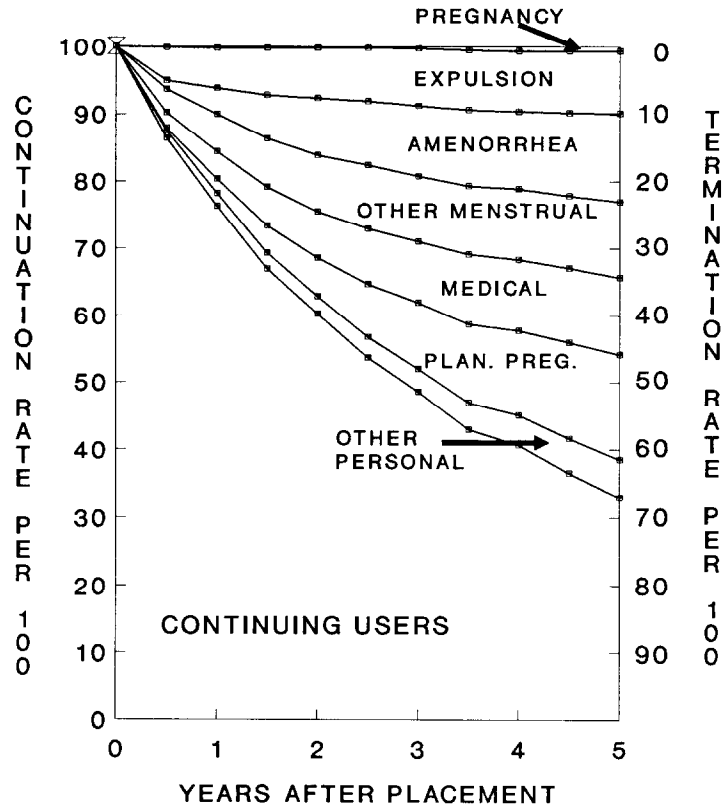
Fundal uterine perforations are often considered insertion-related. There were five fundal perforations, all among users of the LNg 20 device.

Loss to Follow-Up

During the five years, 127 users of the LNg 20 device and 186 women randomized to the TCu 380Ag were lost to follow-up (Table III). They represented 11.3 and 16.8 percent of the original groups.

Pregnancy

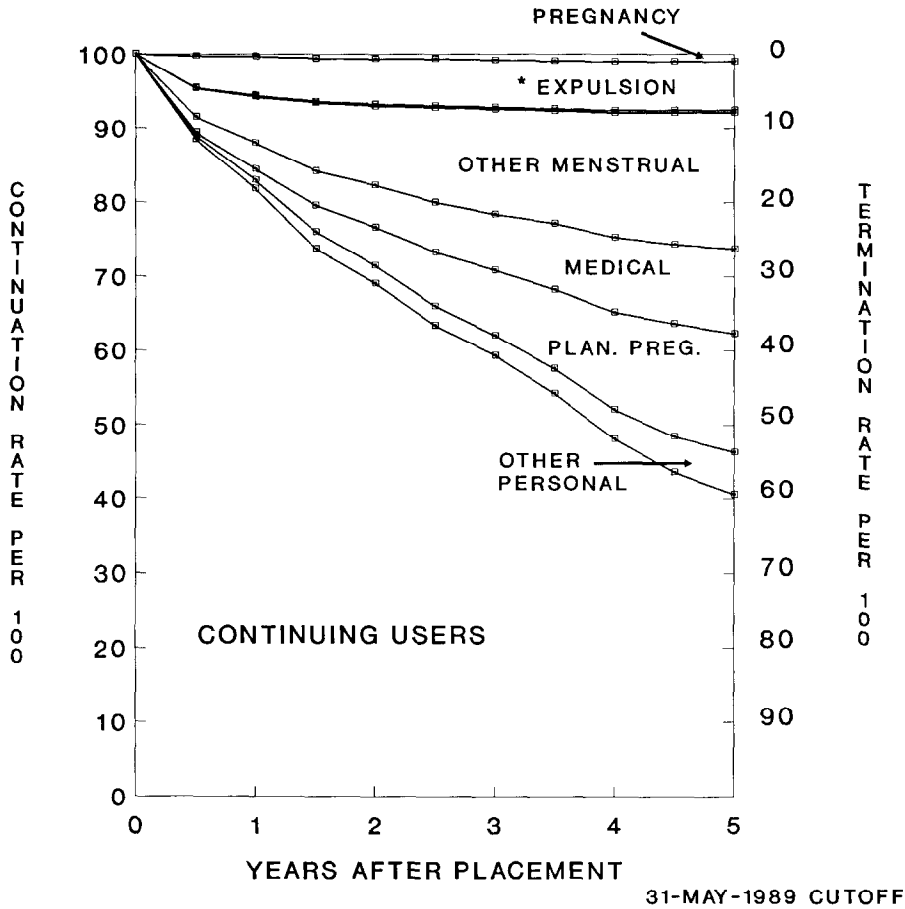
In the first five years following insertion, six users of the LNg 20 device became pregnant as did ten women using the TCu 380Ag device. These data include cases resulting from unnoticed expulsion. Five-year gross pregnancy rates were 1.1±0.5 and 1.4±0.4 for the steroid and copper IUDs, respectively (Table III).



VERTICAL DISTANCE BETWEEN LINES REPRESENTS THE NET CUMULATIVE RATE FOR THE DECREMENT NAMED IN THAT SPACE

31-MAY-1989 CUTOFF

FIG. 1. LEVONORGESTREL IUD 20 μg/d
NET CUMULATIVE TERMINATION RATES BY REASON.



*TERMINATIONS FOR AMENORRHEA CUMULATE TO 0.3 PER 100 AND ARE REPRESENTED BY THE SECOND CURVE UNDER EXPULSION

FIG. 2. TCU 380AG NET CUMULATIVE TERMINATION RATES BY REASON.

Table I: Characteristics at Admission

	Device			
	LNg 20		TCu 380Ag	
Characteristic	Mean	SE	Mean	SE
Age (years)	26.6	0.1	26.7	0.1
Parity (No.)	2.44	0.04	2.40	0.04
Months since last pregnancy	23.7	0.7	24.1	0.8
Hemoglobin (g/dl)	12.7	0.05	12.6	0.04
Menstrual flow (days)	4.2	0.04	4.3	0.04
% Prior IUD use	32.8	1.4	33.6	1.4
% PID before last pregnancy	7.7	0.8	6.4	0.7
% Desire additional children	33.1	1.4	32.4	1.4
No. of Subjects	1124		1121	

No significant differences

Table II: Pain at Insertion: Subject Reports, Intensity Distribution by Device

	Percentage	
Pain	LNg 20	TCu 380Ag
No Pain	34.5	41.3
Minimum	46.7	47.7
Moderate	15.1	9.5
Severe	3.6	1.4
Total	100.0	100.0
N	1124	1121

$X^2 = 33.64$, $P<.0001$

Table III: Five-Year Gross Cumulative Termination Rates by Device

Item	LNg 20 Rate SE	TCu 380Ag Rate SE	No. of Events LNg 20	No. of Events TCu 380Ag
Pregnancy	1.1 ± 0.5	1.4 ± 0.4	6	10
Expulsion	11.8 ± 1.2*	7.4 ± 0.9	99	71
Amenorrhea	19.7 ± 1.6***	0.4 ± 0.2	134	3
Other Menstrual/Pain	15.4 ± 1.4**	23.3 ± 1.6	118	183
Other Medical	16.9 ± 1.5	16.2 ± 1.5	118	113
Planning Pregnancy	25.9 ± 1.9	23.5 ± 1.7	155	153
Other Personal	9.5 ± 1.3	9.4 ± 1.3	56	55
Total Related Terminations	67.0 ± 1.5***	59.4 ± 1.6	686	588
Continuation	33.0 ± 1.5	40.6 ± 1.6	298	335
End of Study Terminations	1.7 ± 0.7	1.0 ± 0.5		
No. Enrolled			1124	1121
No. Lost to Follow-up			127	186
No. of Woman-Years			2,912	3,189

*P<.05 **P<.01 ***P<.001 31 May 1989 Cut-off

A third and a fourth year pregnancy with the Copper T 380Ag device were ectopic. None of the six pregnancies in women with the steroid-releasing IUD was ectopic. With a total of 3189 woman-years in the five-year period, the ectopic pregnancy rate for the Copper T users was 0.6 per 1000 woman-years.

Given the rarity of pregnancies, no trend was observed in annual pregnancy rates for either device; year-to-year variations were not significant. The highest annual pregnancy rate with the LNg 20 device, 0.7±0.4 per 100, was in the fourth year (Table IV), but no pregnancies were observed with this device in the fifth year, which 298 women completed. There were also no pregnancies among users of the LNg 20 device in the second year, completed by 615 women.

Among women contracepting with the TCu 380Ag, the highest annual pregnancy rate, 0.5±0.3 per 100, occurred in the second year (Table IV). There were no fifth year pregnancies among users of the Copper T 380Ag.

Expulsion

First year expulsion rates were about 6.0 per hundred for each device (Table IV). Rates declined monotonically by year for each device with the first year accounting for the majority of all expulsions. Annual expulsion rates were lower for the TCu 380Ag device (Table IV) and cumulative expulsion rates were significantly lower for users of the TCu 380Ag IUD from the end of the third year onwards ($P<.05$). From the second through the fifth year, without regard to the first year's experience, the cumulative expulsion rate of the TCu 380Ag, 1.9±0.5 per 100, was significantly below that of the LNg 20 for the same four-year period, 5.9±1.0 per 100 ($P<.05$).

At the five-year point, cumulative expulsion rates by clinic for the TCu 380Ag device ranged from 4.5 per 100 to 10.8 per 100, while the range with the LNg 20 device was greater, from 6.6 per 100 to 20.7 per 100 (Table V).

Cumulative expulsion rates at five years appeared to decline modestly by parity among users of the TCu 380Ag but to rise somewhat by parity among users of the LNg 20 device (Table VI). Increased age was associated with declining expulsion rates for each device through age 35 (Table VII).

Amenorrhea

Prolonged intervals without menstrual events characterize women's experience with the LNg 20 IUD. Some women requested removal of the IUD after such intervals. By the end of five years, the cumulative termination rate attributed to amenorrhea had reached 19.7±1.6 per 100. Annual termination rates ranged from 2.5 per 100 in year 4 to 6.6 per 100 in year 2 (Table IV). In each clinic the proportion of women who stopped use of the LNg 20 because of amenorrhea was importantly above the number of women with the TCu 380Ag who stopped for this reason. In

Table IV: Gross Annual Rates per 100 by Device and Year

Device	Reason/Rate	Year 1	2	3	4	5
LNg 20	Pregnancy	0.2	0.0	0.2	0.7	0.0
TCu 380Ag	Pregnancy	0.3	0.5	0.2	0.4	0.0
LNg 20	Expulsion	6.3	2.1	1.8	1.2	0.9
TCu 380Ag	Expulsion	5.6	1.0	0.5	0.4	0.0
LNg 20	Amenorrhea	4.5	6.6	3.6	2.5	4.3
TCu 380Ag	Amenorrhea	0.2	0.1	0.0	0.0	0.0
LNg 20	Other Menstrual	6.1	4.1	2.3	1.9	1.9
TCu 380Ag	Other Menstrual	6.7	5.7	5.3	4.8	3.4
LNg 20	Other Medical	4.5	4.0	4.1	2.9	2.7
TCu 380Ag	Other Medical	3.9	2.7	2.8	4.9	3.0
LNg 20	Planning Pregnancy	2.6	5.2	7.5	6.1	7.6
TCu 380Ag	Planning Pregnancy	1.6	4.9	5.6	7.6	6.3
Lng 20	Other Personal	2.2	1.0	1.4	2.3	3.0
TCu 380Ag	Other Personal	1.3	1.6	0.5	2.4	4.0
LNg 20	Continuation	76.3	79.0	80.6	83.6	81.2
TCu 380Ag	Continuation	81.8	84.4	85.9	81.1	84.3

Table V: Variation in Selected 5-Year Cumulative Rates per 100 by Clinic

Reason	LNg 20 Low	LNg 20 High	TCu 380Ag Low	TCu 380Ag High
Expulsion	6.6	20.7	4.5	10.8
Amenorrhea	13.7	35.0	NA	NA
Other Medical Problem	4.7	27.3	6.7	24.3
Continuation	19.8	47.8	18.6	54.2

Significant Within Clinic Variation by Device and Reason

Reason	Clinic	LNg 20	TCu 380Ag	P
Expulsion	Cairo	20.7±3.3	4.5±1.6	<.001
Amenorrhea	All Clinics	-	-	<.01 in each clinic
Other Medical	Santiago	19.1±4.7	6.7±3.0	<.05
Continuation	Santiago	31.3±4.8	53.1±5.1	<.05
Continuation	Campinas	29.0±3.4	41.5±3.6	<.05

Table VI: Five-Year Gross Cumulative Rates by Parity and Device

Rate, Item	Parity 0, 1 LNg	0, 1 380	2 LNg	2 380	3+ LNg	3+ 380
Pregnancy	0.0	2.0	1.5	1.2	1.3	1.1
Expulsion	8.6	8.3	11.8	7.6	13.5	6.4
Amenorrhea	16.2***	0.4	24.2***	0.0	16.8***	0.6
Other Menstrual	13.7	21.3	19.3	21.8	12.2	25.3
Other Medical	17.0	12.7	13.1	19.2	20.1	14.5
Planning Pregnancy	46.4	54.3	26.3	20.0	13.0	8.2
Other Personal	15.7	13.0	8.1	10.5	7.6	7.6
Continuation	24.8	24.4	31.3**	41.2	40.0**	49.8
N, Acceptance	284	290	420	417	419	414

**P<.01 ***P<.001

Table VII: Five-Year Gross Cumulative Rates by Age and Device

Rate, Item	Age <25 LNg	<25 380	25-29 LNg	25-29 380	30-34 LNg	30-34 380	≥35 LNg	≥35 380
Pregnancy	0.8	1.9	1.2	0.8	2.1	2.0	0.0	0.0
Expulsion	13.4	10.1	11.9	7.6	9.8	3.8	10.7	6.2
Amenorrhea	22.4	0.3	19.6	0.3	18.0	0.5	9.4	0.0
Other Menstrual/Pain	18.6	26.4	16.0	21.3	12.3	22.2	15.0	21.9
Other Medical	20.2	16.8	17.6	13.2	13.6	19.7	12.4	13.8
Planning Pregnancy	35.8	38.3	32.5	24.7	9.9	8.8	6.3	4.6
Other Personal	15.4	13.9	8.4	7.3	6.4	8.0	3.4	9.6
Continuation	23.5	28.9	30.0	43.6	46.4	49.2	54.6	54.4
Total Menstrual/Pain	36.8	26.6	32.5	21.5	28.1	22.6	23.0	21.9

P value of significant differences by age within device in Table VII.

Rate	LNg 20	TCu 380Ag
Amenorrhea	.028	NS
Planning Pregnancy	<.001	<.001
Other Personal	.050	NS
Total Terminations and Continuation	<.001	<.001

four clinics cumulative five-year termination rates ascribed to amenorrhea were 14-15 per 100, but were considerably higher in the remaining clinics (Table V). Cumulative termination rates for amenorrhea appeared to decline by age (Table VII). Termination rates for amenorrhea did not correlate with parity. The five-year cumulative termination rate for amenorrhea was 0.4±0.2 per 100 among users of the TCu 380Ag.

Other Menstrual Problems and Pain

In contrast to amenorrhea-induced termination rates, cumulative and annual rates of termination for other menstrual problems and for device-related pain were significantly greater among women with the copper device. At five years, the termination rate from complaints of bleeding and/or pain cumulated to 23.3±1.6 per 100 for women with the TCu 380Ag device as compared with 15.4±1.4 per 100 for users of the LNg 20 ($P<.01$) (Table III). In each study year, the Copper T 380Ag had a higher rate of termination for other menstrual and/or pain complaints than did the LNg 20 device (Table IV).

When all menstrual problems including amenorrhea and pain were jointly considered, the cumulative five-year gross termination rate was 32.3 among women with the LNg 20 and was 23.6 among those assigned the TCu 380Ag device ($P<.01$).

Terminations for Other Medical Reasons

"Other medical reasons" for terminations embrace health-related causes apart from menstrual problems, pain and pregnancy. Cumulative rates of discontinuation for these other medical reasons were 16.2 and 16.9 per 100 at five years for the TCu 380Ag and the LNg 20, respectively (Table III). Annual termination rates ranged between 3-5 per 100 (Table IV). Variation by clinic was notable, however (Table V).

Three categories of medical terminations - device-related effects, reproductive tract infections and possible steroid-related effects - require separate discussion. We consider these in turn.

Five uterine perforations (0.4 percent) were associated with the LNg 20 IUD but none with the TCu 380Ag. The difference missed statistical significance ($.05<P<.10$). Three cases (0.3 percent) of embedded LNg 20 devices were reported. A cervical perforation occurred to a user of the copper device (0.1 percent). Ten women, five using each device, requested removal because of discomfort to their husbands, caused by the device thread. Apart from these events, seven additional device-related removals of the LNg 20 occurred as did five of the TCu 380Ag.

When symptoms suggested PID, investigators confirmed evidence for or ruled out a diagnosis of salpingitis. Removal was required upon confirmation of PID/salpingitis. Upper reproductive tract infections, including PID/salpingitis and endometritis, affected 1.9-2.0 percent of women, with no statistically significant difference found between the

IUDs. The gross five-year cumulative rates of PID were 2.6 and 2.3 per 100 for the steroid and copper devices, respectively. Half of the PID/salpingitis cases were recorded in the initial year.

Because women with prior PID/salpingitis were admitted provided the condition had occurred before their last pregnancy, we analyzed upper reproductive tract infection by PID history (Table VIII). Two percent of women with no history of PID contracted PID/salpingitis or endometritis during five years of IUD use as did 1.9 percent of women who had had such a history before entering the study.

Lower reproductive tract infections led to device removal among 19 women who had received the LNg 20 device and 29 who used the TCu 380Ag ($P>.05$).

Two classes of conditions associated with contraceptive steroids led to termination from the LNg 20 IUD at significantly higher levels than were found among women assigned the TCu 380Ag. These were: (a) skin and hair conditions (acne, hirsutism and other skin conditions); and (b) headaches ($P<.05$) (Table IX). Three other classes of conditions sometimes associated with steroid use - (a) depression and other mood changes, (b) nausea, and (c) weight changes - led to removal of either device at the same rate (Table IX).

Planning Pregnancy and Other Personal Reasons for Termination

At admission 32-33 percent of women desired at least one more child following participation in the study. By the end of five years, termination rates attributed to planning pregnancies were approximately 24-26 per 100 (Table III), with little difference between devices. Planned pregnancy rates declined by age group from a five-year rate of 36-38 per 100 for women less than 25 years old at admission to a five-year rate of 5-6 per 100 among women 35-38 years old at entry to the study (Table VII). Differentials by parity were even stronger. Women with one child discontinued to plan a pregnancy at rates of 46-54 per 100 in the five-year period. In contrast, women with three or more children requested removals for planned pregnancy at cumulative rates of 8-13 per 100 (Table VI). Rates of removal for planning pregnancy were higher in the third through fifth year than in the first two years (Table IV).

"Other" personal reasons for IUD removal comprehend changes in marital status, in residence, family objections to the particular method, etc. The cumulative gross rate was somewhat under 10 per 100 for each device. "Other personal" termination rates tended to decrease with increasing age and increasing parity (Tables VI and VII).

Table VIII: PID/Salpingitis/Endometritis After IUD Insertion (Percentage)

History of PID	Device	Yes	No	Events	N
No History of PID					
	LNg	2.1	97.9	22	1036
	TCu	1.9	98.1	20	1049
	Both	2.0	98.0	42	2085
PID Before	LNg	1.1	98.9	1	87
Last Pregnancy	TCu	2.8	97.2	2	72
	Both	1.9	98.1	3	159

Table IX: Terminations in Years 1-5 Ascribed to Possible Steroid Effects by Device (Percent of Base)

	LNg 20		TCu 380Ag		Statistical
Possible Steroid Effect	N	Percent	N	Percent	Significance
Acne, Hirsutism, Other Skin	6	0.5	0	0.0	<0.05
Headache	18	1.6	2	0.2	<0.001
Depression, Other Mood Changes	2	0.2	2	0.2	NS
Nausea	2	0.2	1	0.1	NS
Weight Change	3	0.3	3	0.3	NS
TOTAL	31	2.8	8	0.7	<0.001

Continuation Rates

An estimated 33.0±1.5 per 100 of the women who had an LNg 20 IUD inserted were still continuing use at the end of five years (Table III). This corresponds to an annual average continuation rate of 80.1 per 100 (geometric mean). The five-year cumulative continuation rate of women who used the copper IUD was significantly higher at 40.6±1.6 per hundred, an annual average rate of 83.5 per 100. Continuation rates for each device increased modestly after the first two years. This tendency reflects the fact that, on average, women who terminate in the first years are younger and of lower parity than those who continue. Median age of users at the end of five years was 34.1 for women with the LNg 20 device and 33.4 for users of the Copper T.

DISCUSSION

This study, which encompasses 6000 woman-years of experience, has documented the remarkable long-term effectiveness of two medicated IUDs. Earlier reports from this study (6,8) and from those of Luukkainen (9), Nilsson and Allonen (10,11) and colleagues in Scandinavian collaborative studies, had demonstrated the effectiveness of the levonorgestrel-releasing device (LNg 20) in randomized shorter term trials. More recently a comparative study in India has shown this steroid-releasing IUD to be effective through three years of use (12). With a gross cumulative five-year pregnancy rate of 1.1±0.5 per 100 in the present study, this device is, at worst, as effective as the most effective intrauterine device yet reported (13,14). Although the data base is yet too slim for certitude, the age-specific pregnancy rates observed in this study suggest that the steroid-releasing device may have effectively abolished the well established inverse correlation of pregnancy rates with age found in most large-scale IUD studies of non-medicated and copper IUDs. The few pregnancies among users of the TCu 380Ag also do not demonstrate age effects in this study, although these were manifest in earlier U.S. studies (15).

The contraceptive effectiveness of the LNg 20 device was essentially matched by the TCu 380Ag with a five-year cumulative pregnancy rate of 1.4 per 100 that was not statistically distinguishable from that of the LNg 20 device. The effectiveness of the copper device also matched the five-year pregnancy rate found by WHO for the TCu 380A (14). The U.S. four-year study of Sivin and Tatum, however, shows a rate twice as high (16). That study was concentrated among women under age 25, which likely accounts for the higher pregnancy rate (13).

The two IUDs have demonstrated remarkable long-term effectiveness and good acceptability. Each device had lower first segment gross cumulative pregnancy rates at five years than have been reported in long-term randomized comparative trials for any reversible method of contraception, including NORPLANT® capsule implants or NORPLANT®-2 implants. Indeed, the LNg 20 device releases drug into the uterus in the same manner that NORPLANT®-2 device releases the same drug into the arm. Because the intrauterine device has local contraceptive effects, a

lower release rate than is needed for implants achieves effectiveness. The performance of the LNg 20 IUD seems unaffected by the weight of the women, unlike the performance of NORPLANT® and vaginal rings releasing 20 µg of levonorgestrel (17). The five-year cumulative pregnancy rate of the LNg 20 IUD is one-third that of the one-year pregnancy rate of the vaginal rings which release the same daily dose of the same drug (17). The copper-releasing IUD is also unaffected by weight, but its effectiveness, as indicated in other studies, is modestly affected by age.

Secondary acceptability, measured by continuation, appeared to differ between devices. Continuation rates of Copper IUD users were significantly higher than those of the LNg 20 device users. In each of the first three study years, copper IUD users had continuation rates 5 per 100 higher than did women with the steroid device. Neither age nor parity differences could account for this. In the fourth and fifth year, continuation rates were about the same for the two devices. In comparative Scandinavian studies of copper and levonorgestrel devices (9-11), however, differentials in continuation between steroid and copper devices appear to be minimal. On the other hand, Indian women using the LNg 20 had markedly lower continuation rates through three years than did their compatriots randomly assigned to use copper devices. This was attributed to amenorrhea terminations (12). Variation in counselling concerning device-related amenorrhea, spotting and other problems undoubtedly occurred in the different studies and clinics, but the results also indicate differences arising from the several cultural backgrounds represented.

Counselling about amenorrhea during use of the LNg 20 is necessary prior to insertion and in the first months to reassure women that the absence of bleeding does not signify pregnancy. Counselling is also required for persistent amenorrhea. Some women need reassurance that the amenorrhea is reversible, and that it does not signal a loss of reproductive function. In some cultures counselling and reassurance is required to dispel the notion that the woman is retaining "bad blood", and is thereby injuring herself. Failure to reassure subjects satisfactorily on one or all three counts undoubtedly reflects in termination rates for amenorrhea. Counselling about amenorrhea should indicate that the LNg 20 IUD is associated with increased hemoglobin levels (6,8).

Two percent of participants experienced PID/salpingitis/endometritis and had to have devices removed during the five-year course of use. Half the cases occurred during the first year, a pattern that is well known. Women who have become pregnant after an episode of PID and then entered the study were not at higher risk of contracting the disease than were other IUD users. The Pearl index for PID for each device was 0.7 per 100 woman-years. Fecundity has returned to normal levels after removal of the studied IUDs (18).

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