FERTILITY AND STERILITY®
VOL. 72, NO. 3, SEPTEMBER 1999

Published by Elsevier Science Inc.
Printed on acid-free paper in U.S.A.

INCAP Publication DCI/017

The World Health Organization Multinational Study of Breast-feeding and Lactational Amenorrhea. III. Pregnancy during breast-feeding

*World Health Organization Task Force on Methods for the Natural Regulation of Fertility**

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Objective: To determine the risk of pregnancy during lactational amenorrhea relative to infant feeding status.

Design: Prospective longitudinal study.

Setting: Five developing and two developed countries.

Patient(s): Four thousand one hundred eighteen breast-feeding mother-infant pairs.

Intervention(s): Infant feeding practices, menstrual status, and pregnancy were measured.

Main Outcome Measure(s): Life-table rates of pregnancy.

Result(s): In the first 6 months after childbirth, cumulative pregnancy rates during amenorrhea, depending on how the end of amenorrhea was defined, ranged from 0.9% (95% confidence interval [CI] = 0%–2%) to 1.2% (95% CI = 0%–2.4%) during full breast-feeding, and from 0.7% (95% CI = 0.1%–1.3%) to 0.8% (95% CI = 0.2%–1.4%) up to the end of partial breast-feeding. At 12 months, the rates ranged from 6.6% (95% CI = 1.9%–11.2%) to 7.4% (95% CI = 2.5%–12.3%) during full breast-feeding, and from 3.7% (95% CI = 1.9%–5.5%) to 5.2% (95% CI = 3.1%–7.4%) up to the end of partial breast-feeding.

Conclusion(s): These results support the Bellagio Consensus on the use of lactational amenorrhea for family planning, and confirm that the lactational amenorrhea method is a viable approach to postpartum contraception. (Fertil Steril® 1999;72:431–40. ©1999 by American Society for Reproductive Medicine.)

Key Words: Breast-feeding, lactation, infant feeding, amenorrhea, fertility, pregnancy, postpartum contraception, lactational amenorrhea method, LAM, international

Received October 6, 1998; revised and accepted March 23, 1999.

Supported by United Nations Development Programme/United Nations Population Fund/World Health Organization/World Bank Special Programme of Research, Development and Research Training in Human Reproduction, Geneva, Switzerland.

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* See Appendix A.

0015-0282/99/$20.00
PII S0015-0282(99)00274-5

Breast-feeding is associated with the suppression of ovarian activity and thus with a variable period of amenorrhea and infertility (1). The risk of the resumption of fertility, and therefore of conception, during lactation is related to infant feeding patterns. Women who breast-feed their infants frequently and who delay the introduction of supplementary feedings tend to remain amenorrheic for a longer period (2, 3). A consensus meeting held in Bellagio, Italy in 1988 (4, 5) postulated that full or nearly full breast-feeding during lactational amenorrhea confers 98% protection against pregnancy in the first 6 months after childbirth. This degree of protection has been shown to be valid in several clinical studies (6–8). Although these clinical trials involved up to 485 women who were prospectively using the lactational amenorrhea method (LAM) (9) to avoid pregnancy, each study involved a homogeneous group of breast-feeding women, and one study (6) involved extraordinary support for breast-feeding. One multinational study concurred with these results but involved small numbers of women at each center (10).

A large prospective study was conducted to determine the relation between infant feeding practices and the duration of amenorrhea (11). This study also measured the occurrence of pregnancy among women in five developing and two developed countries. The purpose of this analysis was to determine the rate of pregnancy during lactational amenorrhea according

to infant feeding status among women in this multinational study to support or refute advice to breast-feeding women about the efficacy of lactational amenorrhea as a period of significant protection from pregnancy. This analysis has the following advantages: it includes a far larger number of women than has been studied similarly in the past, and no attempt was made to alter the indigenous infant feeding behaviors of the women who participated.

MATERIALS AND METHODS

Subjects and Procedures

Seven study centers participated in this research. They were located in Chengdu, China; Guatemala City, Guatemala; Melbourne/Sydney, Australia; New Delhi, India; Sagamu, Nigeria; Santiago, Chile; and Uppsala, Sweden. A total of 4,118 women were recruited into the study. The first participants were admitted in April 1989 and the last completed the study in December 1993. All were aged between 20 and 37 years at the time of entry into the study, had breast-feeding experience, and were literate. None was planning to use a hormonal method of contraception after childbirth, and all intended to breast-feed for at least 6 months. Women with a history of irregular menstrual cycles (<21 or >35 days) or of infertility were not recruited. The infants were all singletons who were delivered vaginally at term (≥37 weeks) and were above the 10th percentile in birth weight (or ≥2.5 kg if norms for the population were unavailable).

Mothers were admitted to the study within 7 days of childbirth. Each woman kept a daily record of the number of breast-feeding episodes and the number and type of any other foods or fluids (supplementary feedings) given to the infant. Days during which vaginal bleeding or spotting occurred also were recorded. For 24 hours every 2 weeks, a detailed record chart was completed in which the timing and duration of breast-feeding episodes were recorded, together with the details of supplementary feedings. Every 2 weeks, mothers were visited at home, where the feeding diaries were checked. At this visit, they were asked whether they had had intercourse since the previous visit and what method of contraception they were using (if any).

The return of fertility was the end point of the study. Because the detection of ovulation or measurement of hormone concentrations would have been impractical in a study of this size, the reappearance of regular cyclicity or the occurrence of pregnancy were regarded as proxies for the return of fertility. Thus, participation in the study continued until the woman experienced what she considered to be two normal menstrual periods or until conception occurred, whichever came first. At each follow-up visit, mothers were asked whether they thought they were pregnant. If the answer was "yes," arrangements were made to confirm the pregnancy, with a pregnancy test and/or an ultrasound examination.

Mothers who started using any hormonal method of contraception were discontinued from the study from the date of the introduction of such a method. The study protocol permitted the use of nonhormonal methods, but in the pregnancy analysis, the experience of users of such methods was restricted to the period before their introduction.

This study was approved by the World Health Organization Secretariat Committee on Research Involving Human Subjects. Local ethics committee approval also was obtained in all centers, and all women participating in the study gave informed consent.

Definitions

Bleeding Episode

Bleeding per vaginam that lasted at least 2 days and required the use of sanitary protection for at least 1 day was defined as a menstrual bleeding episode. Bleeding episodes that occurred within 2 weeks of the end of lochia or that were associated with a gynecologic procedure, such as the insertion of an intrauterine device, were ignored.

Confirmed First Menses—Human Reproduction Programme Rule

A bleeding episode was confirmed as a first menses only if a second bleeding episode (meeting the same requirements listed earlier) occurred within the next 21–70 days. If a second episode occurred outside these time limits, the first episode was ignored and the second episode was defined as the first menses. Only one bleeding episode could be discounted. In this way, the first menses was "confirmed" by the "HRP rule" (named for the Human Reproduction Programme of the World Health Organization that created this algorithm for the study). A bleeding episode also could be confirmed as the first menses if conception occurred within the next 6–55 days, on the grounds that had conception not occurred, there would have been a second bleeding episode within 21–70 days. The main operational definition of the end of lactational amenorrhea in this study was the date of the confirmed first menses by the HRP rule.

During breast-feeding, a bleeding episode can occur as a consequence of ovarian follicular development followed by the withdrawal of estrogen (i.e., in the absence of ovulation). Bleeding also can follow ovulation with inadequate luteinization. Early "menstrual cycles" in breast-feeding women can be extremely irregular, indicating that ovarian activity is present but fecundity has not been restored. The HRP rule was created to more closely approximate the true return of fertility and not just the return of menses. By "confirming" that the first menses is part of a cyclic pattern, the HRP rule allows isolated bleeding episodes reflective of ovarian activity, but not true fertility, to be ignored.

All First Menses—HRP Rule

If the subject had one bleeding episode but discontinued participation in the study before the episode could be con-

firmed as a first menses by the HRP rule, this first "unconfirmed" menses was added to the confirmed first menses described earlier to comprise all first menses. Thus, this second operational definition of the end of lactational amenorrhea included all the cases of confirmed first menses but avoided the loss of cases in which a bleeding episode probably marked the return of fertility but the women were not observed long enough to confirm this. Undoubtedly, in some cases, this definition abbreviated the period of amenorrhea that would have been seen if the women had been followed up for a longer period.

All First Bleeding Episodes

Because all bleeding episodes during the study were recorded, the end of amenorrhea also was defined as the date of the onset of the first bleeding episode, regardless of whether it qualified as a menses by the HRP rule. Thus, a third operational definition of the end of amenorrhea was studied, namely the first-ever bleeding episode. Although this definition included episodes of bleeding that clearly were not indicative of the return of fertility, this definition was included to compare the findings of this analysis with the results of other research. Other studies have defined the end of amenorrhea as the first bleeding episode without attempting to interpret the meaning of the bleeding in terms of the degree of fertility that it represents.

The Woman's Perception of the First Menses

Finally, concerning each bleeding episode, the women were asked whether they perceived the bleeding to be more, less, or the same in amount as a normal menses. Thus, a fourth definition of the end of amenorrhea was explored, namely the first time that a woman perceived that the bleeding episode was a "normal" menses (i.e., that the amount of bleeding was the same or more than her former menses). This definition was called the woman's perception of the first menses.

Breast-feeding Status

Breast-feeding status at the estimated time of conception in the women who became pregnant was defined in terms of three categories: full breast-feeding, in which the infant received only breast milk directly from the mother's breast and no other liquid or solids, or in which the infant received water and other noncaloric fluids or tastes of caloric supplements, vitamins, or medicine in addition to breast-feeding; partial breast-feeding, in which caloric supplements were given in amounts greater than tastes; and weaned, in which the infant was no longer being breastfed.

A more detailed description of the subjects, methods, and definitions used in this study was given in an earlier publication (11).

TABLE 1

Number of pregnancies during the study by breast-feeding status at the estimated time of conception, by contraceptive use at the estimated time of conception, and by study center.

	Breast-feeding status at conception						
	Full		Partial		Weaned		
	Contraceptive use		Contraceptive use		Contraceptive use		
Study center	No	Yes	No	Yes	No	Yes	Total
Chengdu	13	2	7	2	2	3	29
Guatemala City	—	—	9	7	0	1	17
Melbourne/Sydney	—	—	5	4	3	2	14
New Delhi	1	0	4	2	2	0	9
Sagamu	—	—	—	—	3	2	5
Santiago	—	—	2	0	1	0	3
Uppsala	—	—	5	1	1	1	8
All centers	14	2	32	16	12	9	85

Note: Numbers represent the number of pregnancies.

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Statistical Analyses

The median time until the start of intercourse and the use of contraceptives was calculated using survival analysis (12).

Survival analysis also was used to calculate cumulative pregnancy rates and their SEs during amenorrhea and up to the end of full and partial breast-feeding, with adjustment for the occurrence of sexual intercourse (i.e., including only those periods when intercourse was reported). The observed times for a subject were censored when she reached the end of amenorrhea; when she reached the end of each breast-feeding category; when she started using a method of contraception (coitus interruptus was included as a method), assuming that women were continuously protected by their method; and when she withdrew from the study. The rates were compared by χ^2 test.

RESULTS

In all, 3,422 women completed the study with a recognized fertility outcome: 3,337 were regarded as having had two menstrual bleeding episodes and 85 became pregnant. The remaining 696 women had only one (i.e., unconfirmed) menstrual bleeding episode before leaving the study (n = 150) or left the study before they had even one bleeding episode (n = 546).

Table 1 shows the distribution of the 85 pregnancies that occurred during the study according to study center, breast-feeding status at the estimated time of conception, and use of a family planning method at the estimated time of conception. One third of all pregnancies reported in the study

TABLE 2

Number of pregnancies during (versus after) amenorrhea among breast-feeding women who were not using contraception according to four definitions of the end of amenorrhea, by study center.

Study center	End of amenorrhea* according to the indicated definition				
	HRP rule				
	Confirmed first menses during amenorrhea (after amenorrhea)	All first menses during amenorrhea (after amenorrhea)	Woman's perception of first menses during amenorrhea (after amenorrhea)	First reported bleeding episode during amenorrhea (after amenorrhea)	Total†
Chengdu	18	15	16	15	20
	(2)	(5)	(4)	(5)	
Guatemala City	4	3	4	3	9
	(5)	(6)	(5)	(6)	
Melbourne/Sydney	2	2	5	2	5
	(3)	(3)	(0)	(3)	
New Delhi	2	1	2	1	5
	(3)	(4)	(3)	(4)	
Sagamu	0	0	0	0	0
	(0)	(0)	(0)	(0)	
Santiago	1	0	1	0	2
	(1)	(2)	(1)	(2)	
Uppsala	4	4	4	4	5
	(1)	(1)	(1)	(1)	
All centers	31	25	32	25	46
	(15)	(21)	(14)	(21)	

Note: HRP = human reproduction programme.

* See text for definitions.

† Total number of breast-feeding women who were not using contraception at the estimated time of conception.

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occurred in one center (Chengdu). Twenty-one women conceived after the infant had been totally weaned, leaving 64 women who became pregnant during breast-feeding. The cases of pregnancy after weaning are not considered further, as the focus of this analysis is pregnancy during lactation.

Among the 64 pregnancies that occurred during lactation, one fourth (n = 16) occurred during full breast-feeding and three fourths (n = 48) occurred when the infant was receiving caloric food supplements of varying amounts (i.e., during partial breast-feeding). Nearly all the pregnancies that occurred during full breast-feeding (15 of the 16) were in one center (Chengdu).

Among the 64 women who conceived while breast-feeding, 18 reported using a family planning method during the estimated time of conception, leaving 46 pregnancies that occurred among breast-feeding women who were not using contraception. Contraceptive failure was associated with the use of withdrawal, natural methods of family planning, barrier methods, intrauterine devices, and vasectomy. About half the contraceptive failures occurred after the women clearly were already cycling (i.e., menstruating by the confirmed first menses—HRP rule).

Conceptions During Lactational Amenorrhea

Table 2 shows the distribution of the 46 pregnancies that occurred among breast-feeding women who were not using contraception according to whether the pregnancy occurred during amenorrhea as per each of the four definitions of the end of amenorrhea. When the confirmed first menses—HRP rule was used to define the end of amenorrhea, 31 pregnancies (67%) among breast-feeding women who were not using contraception occurred during amenorrhea. However, when all first menses—HRP rule or first reported bleeding episode was used to define the end of amenorrhea, only 25 pregnancies (54%) occurred during amenorrhea. This is to be expected, because when bleeding episodes that are not confirmed to be cyclic mark the end of amenorrhea, the period of amenorrhea is shortened.

When the end of amenorrhea was defined as the woman's perception of the first menses, the number of pregnancies that occurred during amenorrhea was almost the same as when the confirmed first menses rule was used. However, this is just a coincidence because the women who became pregnant during amenorrhea are somewhat different under the two definitions. Women frequently reported vaginal bleeding episodes that they did not describe as normal menses.

TABLE 3

Six-month cumulative pregnancy rates during lactational amenorrhea up to the end of full breast-feeding.

	End of amenorrhea according to the indicated definition			
	HRP rule			
Study center	Confirmed first menses only	All first menses	Woman's perception	First reported bleeding episode
Chengdu	1.8 (0–3.5)	1.4 (0–2.9)	1.4 (0–2.9)	1.4 (0–3.0)
Woman-months	1,390	1,388	1,374	1,364
Guatemala City	0	0	0	0
Woman-months	93	93	88	86
Melbourne/Sydney	0	0	0	0
Woman-months	742	742	753	707
New Delhi	0	0	0	0
Woman-months	356	353	327	307
Sagamu	0	0	0	0
Woman-months	13	13	13	13
Santiago	0	0	0	0
Woman-months	78	78	79	70
Uppsala	0	0	0	0
Woman-months	297	296	305	284
All centers	1.2 (0–2.4)	0.9 (0–2.0)	0.9 (0–2.0)	1.0 (0–2.1)
Woman-months	2,969	2,963	2,939	2,831

Note: Values are percentages, with 95% confidence intervals in parentheses. Cumulative pregnancy rates were censored at the initiation of contraception and adjusted for exposure to coitus during each fortnight. HRP = Human Reproduction Programme.

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Rates of Pregnancy During Lactational Amenorrhea

Cumulative pregnancy rates at 6 months after childbirth during lactational amenorrhea up to the end of full and partial breast-feeding are shown in Tables 3 and 4, respectively. The corresponding rates at 12 months after childbirth are shown in Tables 5 and 6. The breast-feeding categories are used cumulatively so that, for example, for all centers combined, in the 6-month life table using the confirmed first menses definition, the 5,639 woman-months of exposure up to the end of partial breast-feeding (Table 4) includes the 2,969 months of exposure during full breast-feeding in Table 3.

All Centers Combined

For all centers combined, women who were still breast-feeding and remained amenorrheic (according to the HRP-confirmed first menses definition) at the end of 6 months had a cumulative pregnancy rate of 0.8% (95% confidence interval [CI] = 0.2%–1.4%), whereas at the end of 12 months, they had a cumulative pregnancy rate of 4.4% (95% CI = 2.5%–6.3%).

The cumulative pregnancy rates calculated from delivery until the end of full breast-feeding and from delivery until the end of partial breast-feeding were not significantly different ($P<.05$) at either time limit (6 or 12 months). However, for each breast-feeding status, the pregnancy rate at 12 months postpartum was substantially higher than that at 6 months postpartum.

There were no statistically significant differences in pregnancy rates among the various definitions of the end of amenorrhea at either 6 or 12 months. Although the various definitions of the end of amenorrhea yielded different numbers of women who became pregnant before the return of menses (Table 2), these different numerators did not result in significantly different rates of pregnancy.

Center Differences

Among the individual centers, as seen in Tables 3 and 5, there were no pregnancies during amenorrhea and full breast-feeding in any center except Chengdu. Thus, the pregnancy rates during full breast-feeding are entirely a reflection of one center.

The 6-month pregnancy rate during partial breast-feeding and lactational amenorrhea was notably high in Uppsala at 3.2% (95% CI = 0%–7.8%). No pregnancies were reported in the other developed country (Melbourne/Sydney) under these conditions.

In Santiago, no pregnancies were reported during amenorrhea except when amenorrhea was defined according to the woman's perception. Using the woman's perception of the first menses, the pregnancy rate during partial breast-feeding

TABLE 4

Six-month cumulative pregnancy rates during lactational amenorrhea up to the end of partial breast-feeding.

Study center	End of amenorrhea according to the indicated definition			
	HRP rule			
	Confirmed first menses only	All first menses	Woman's perception	First reported bleeding episode
Chengdu	1.1 (0–2.2)	0.9 (0–1.8)	0.9 (0–1.9)	0.9 (0–1.9)
Woman-months	1,937	1,934	1,910	1,900
Guatemala City	0.7 (0–2.1)	0.7 (0–2.2)	0.7 (0–2.2)	0.8 (0–2.5)
Woman-months	812	799	801	723
Melbourne/Sydney	0	0	0	0
Woman-months	1,109	1,109	1,131	1,053
New Delhi	0	0	0	0
Woman-months	731	721	665	610
Sagamu	0	0	0	0
Woman-months	281	281	277	272
Santiago	0	0	4.3 (0–12.4)	0
Woman-months	258	254	263	229
Uppsala	3.2 (0–7.8)	3.2 (0–7.8)	3.1 (0–7.4)	3.5 (0–8.4)
Woman-months	511	511	521	481
All centers	0.8 (0.2–1.4)	0.7 (0.1–1.3)	0.8 (0.2–1.4)	0.8 (0.1–1.4)
Woman-months	5,639	5,609	5,568	5,268

Note: Values are percentages, with 95% confidence intervals in parentheses. Cumulative pregnancy rates were censored at the initiation of contraception and adjusted for exposure to coitus during each fortnight. HRP = Human Reproduction Programme.

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TABLE 5

Twelve-month cumulative pregnancy rates during lactational amenorrhea up to the end of full breast-feeding.

Study center	End of amenorrhea according to the indicated definition			
	HRP rule			
	Confirmed first menses only	All first menses	Woman's perception	First reported bleeding episode
Chengdu	7.8 (2.7–12.9)	7.4 (2.4–12.5)	8.4 (3.0–13.7)	7.7 (2.5–13)
Woman-months	1,706	1,704	1,682	1,669
Guatemala City	0	0	0	0
Woman-months	95	95	90	88
Melbourne/Sydney	0	0	0	0
Woman-months	762	761	772	725
New Delhi	0	0	0	0
Woman-months	362	358	331	309
Sagamu	0	0	0	0
Woman-months	13	13	13	13
Santiago	0	0	0	0
Woman-months	79	79	80	73
Uppsala	0	0	0	0
Woman-months	298	298	307	285
All centers	6.8 (2.1–11.5)	6.6 (1.9–11.2)	7.4 (2.5–12.3)	6.9 (2.0–11.8)
Woman-months	3,315	3,308	3,275	3,162

Note: Values are percentages, with 95% confidence intervals in parentheses. Cumulative pregnancy rates are censored at the initiation of contraception and adjusted for exposure to coitus during each fortnight. HRP = Human Reproduction Programme.

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TABLE 6

Twelve-month cumulative pregnancy rates during lactational amenorrhea up to the end of partial breast-feeding.

Study center	End of amenorrhea according to the indicated definition			
	HRP rule			
	Confirmed first menses only	All first menses	Woman's perception	First reported bleeding episode
Chengdu	5.8 (2.7–8.8)	5.1 (2.2–8)	5.6 (2.5–8.7)	5.3 (2.3–8.3)
Woman-months	2,934	2,930	2,867	2,844
Guatemala City	4.2 (0–9.1)	2.3 (0–5.8)	6 (0–12)	2.8 (0–6.8)
Woman-months	1,159	1,132	1,128	998
Melbourne/Sydney	2.6 (0–7.6)	2.6 (0–7.7)	5.3 (0–11.4)	2.8 (0–8.3)
Woman-months	1,517	1,517	1,556	1,427
New Delhi	5.5 (0–13.4)	3.8 (0–11)	6.5 (0–15.8)	4.8 (0–13.9)
Woman-months	960	950	854	788
Sagamu	0	0	0	0
Woman-months	506	504	486	480
Santiago	0	0	4.3 (0–12.4)	0
Woman-months	323	313	326	271
Uppsala	5.4 (0–11.6)	5.4 (0–11.6)	5.2 (0–11)	5.9 (0–12.6)
Woman-months	634	633	652	599
All centers	4.4 (2.5–6.3)	3.7 (1.9–5.5)	5.2 (3.1–7.4)	4.1 (2.1–6.1)
Woman-months	8,033	7,979	7,869	7,407

Note: Values are percentages, with 95% confidence intervals in parentheses. Cumulative pregnancy rates are censored at the initiation of contraception and adjusted for exposure to coitus during each fortnight. HRP = Human Reproduction Programme.

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and amenorrhea was 4.3% at both 6 and 12 months (95% CI = 0%–12.4%).

Resumption of Sexual Relations

In all centers except Sagamu, women started having intercourse on average when the infant was about 6–8 weeks old (Table 7). In Sagamu, where a period of postpartum abstinence is traditional, the median time for the resumption of intercourse was >17 weeks postpartum. Women were not asked how often they had intercourse but simply whether it had occurred since the previous follow-up visit. Women in Chengdu reported intercourse significantly more often ($P<.001$) than women in any other center: intercourse was reported during >82% of the follow-up interviews.

Use of Contraception

Women who intended to use a hormonal method of contraception after childbirth were not recruited to the study and those who started to use hormonal contraception during the course of the study (n = 107) were discontinued. For those women who initiated the use of nonhormonal contraception during amenorrhea, the median time to the start of contraceptive use is shown in Table 8. In Uppsala and Melbourne/Sydney, >70% of these women started using a barrier method of contraception, as did >50% of the women in Guatemala City, New Delhi, and Sagamu. More than 90% of these women in Santiago and 48% in Chengdu used an intrauterine device. Female sterilization was common in New Delhi (26.4%) and Guatemala City (11%), whereas in Chengdu, the partners of 50% of the women who initiated the use of contraception during the study underwent vasectomy. Withdrawal was used commonly in Sagamu (29.4%), Guatemala City (11.7%), and Uppsala (9.9%).

TABLE 7

Median time to the start of intercourse and percentage of 2-week intervals during which intercourse occurred since admission to the study and since the start of intercourse, by center.

Study center	Median time to the start of intercourse		Percentage of 2-week intervals during which intercourse occurred	
	No. of days	95% confidence interval	Since admission to study	Since resumption of coitus
Chengdu	42	40.9–43.1	82.1	99.2
Guatemala City	40	38–41.5	58.4	80.6
Melbourne/Sydney	52	51.5–53	69.3	81.7
New Delhi	52	51–52	62.4	92.4
Sagamu	122	108–137	47.5	81.0
Santiago	51	50.5–52	62.1	86.2
Uppsala	53	51–54	61.2	79.5

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TABLE 8

Percentage of women who were not using contraception before their first menses and the median time to the initiation of contraceptive use among users, by study center.

Study center	Percentage of women who were not using contraception	Median time to initiation of contraceptive use	
		No. of days	95% CI
Chengdu	68.4	126	110–165
Guatemala City	58.1	52	51–53
Melbourne/Sydney	46.3	51	48–56
New Delhi	61.7	44	39–52
Sagamu	59.4	81	79–93
Santiago	17.2	39	39–40
Uppsala	31.3	56	55–68

Note: The first menses was defined as the confirmed first menses—Human Reproduction Programme rule. CI = confidence interval.

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DISCUSSION

Pregnancy rates during lactational amenorrhea of 5%–10% (without regard for time postpartum) have been reported consistently in demographic studies (13, 14). Estimates of the risk of pregnancy during amenorrhea calculated from ovulation rates have varied from 0.9% (15) to 1.7% (16) at 6 months, figures that are in close agreement with the findings of this study. In this study, the cumulative pregnancy rates ranged from 3.7% (95% CI = 1.9%–5.5%) to 7.4% (95% CI = 2.5%–12.3%) among amenorrheic women at 12 months, findings that are in agreement with the estimate of 7% made by Short et al. (16) in a study of Australian women, but lower than the estimate of 17.2% made by Diaz et al. (15) in a study of women from Santiago, Chile.

The overall rates of pregnancy observed herein during lactational amenorrhea until the end of full breast-feeding did not differ significantly from those until the end of partial breast-feeding, at either 6 or 12 months. The pregnancy rate had been expected to increase from the full to the partial category of breast-feeding because previous research linked breast-feeding frequency and the delay of supplementation to the duration of lactational infertility. The dose-response was not seen when the centers were combined because of the pregnancies that occurred during lactational amenorrhea in the full breast-feeding category (all of which occurred in Chengdu).

Mothers in Chengdu were more sexually active and avoided supplementing for a longer period than generally recommended; this period was longer than that in all the other centers. However, actual breast-feeding behavior in Chengdu during full breast-feeding appeared to be reduced compared with the other centers (11). The mean total duration of suckling was lowest in Chengdu during the first 6 postpartum months, and at no time during amenorrhea did infants in Chengdu spend more than a mean total duration of 80 minutes per day at the breast (11).

Some investigators (17, 18) have suggested that there may be a threshold for suckling duration per day that is required for nipple stimulation to maintain suppression of the hypothalamic-pituitary axis, and that when suckling duration falls below this threshold, the risk of ovulation and therefore of pregnancy increases. Finally, it is important to remember that the breast-feeding status reported here (i.e., full or partial breast-feeding) is actually an index of the degree to which the infants were given supplements and not some amount of breast-feeding (see definition). Thus, this analysis more accurately supports conclusions about how much supplementation can be tolerated than about how much breast-feeding stimulation is required.

The comparatively high 6-month pregnancy rate seen in Uppsala during amenorrhea and partial breast-feeding was characterized by a wide confidence interval because of the comparatively small number of woman-months of exposure. In Melbourne, the closest comparison group, no pregnancies occurred under the same conditions and the exposure time was nearly double that in Uppsala.

The pregnancies seen in Santiago only when the woman's perception of the first menses was used to define the end of amenorrhea suggests that this somewhat subjective measure of the return of menses may not be appropriate for use with the LAM. All the other definitions applied in Santiago resulted in pregnancy rates during amenorrhea of zero. As in Uppsala, the confidence interval of the pregnancy rate was wide, owing at least in part to the small number of woman-months of exposure.

Small numbers of woman-months of exposure to pregnancy were seen in Sagamu and in Santiago. These were due to censoring for lack of sexual activity and for contraceptive use, respectively.

Care was taken in this study to define the end of amenorrhea carefully and to consider whether any one definition of the first menses would be associated with a higher or lower rate of pregnancy during amenorrhea; however, no difference in the rate of pregnancy during lactational amenorrhea was found when the various definitions were compared. Thus, although a careful interpretation of the meaning of a bleeding episode (i.e., the HRP-confirmed first menses) resulted in a longer duration of amenorrhea and a correspondingly higher number of pregnancies, the corresponding pregnancy rate was not significantly higher than when a simpler definition of menses (i.e., the first reported bleeding episode) was used. By the latter, simpler definition, the duration of amenorrhea is shorter, and more months of unnecessary contraceptive use would result if women started

to use contraception at the end of amenorrhea. However, the simpler definition may have more programmatic and personal acceptability, and women may find double protection to be acceptable in the face of early unexplained bleeding episodes. In this discussion, however, the illustrations of the pregnancy rates generally use the HRP-confirmed first menses to define the end of amenorrhea because this definition resulted in the greatest period of exposure to pregnancy during amenorrhea, presenting a "worst-case" scenario.

The Bellagio Consensus (4, 5) led to the development of the LAM of family planning (9), which advises that a woman has a cumulative risk of pregnancy of <2% if she is amenorrheic and fully or nearly fully breast-feeding as long as the infant is still <6 months old. If any of these three conditions is not met, she is advised to use a method of family planning that does not interfere with breast-feeding. For all centers combined, the highest 6-month cumulative pregnancy rate among women who were fully breast-feeding, amenorrheic, and not using contraception in this multicenter study was 1.2% (95% CI = 0%–2.4%). Thus, this study confirms the Bellagio Consensus (19).

It is important to note that the women in this study were not using the LAM. Indeed, the method had not been created until after this study was begun. Women who are proactively trying to avoid pregnancy through good breast-feeding practices and the recognition of the return of menses may behave differently than women who are simply breast-feeding their infants. Therefore, the efficacy of the LAM is only simulated in this study.

However, it can be argued that the efficacy of the LAM would be better in actual use than in simulated analyses of observed breast-feeding behaviors because users of the LAM learn the breast-feeding behaviors that maximize milk production (and, simultaneously, the duration of lactational amenorrhea) when they learn the LAM algorithm (9). The fact that contemporary breast-feeding practices were studied herein (i.e., there was no attempt to change existing breast-feeding behaviors) suggests that the rates produced may underestimate the pregnancy protection during actual use of the LAM.

The extent to which women in this study represent likely LAM users is not clear. All mothers previously had breastfed an infant for at least 4 months and intended to breast-feed the study infant for at least 6 months. To date, the studies of LAM efficacy suffer from the drawback of including only women with breast-feeding experience. It is reasonable to characterize typical LAM users as women who intend to breast-feed for at least 6 months, but the effect of previous breast-feeding experience on current LAM performance is unknown.

Short et al. (16) recommended extending the Bellagio or LAM guidelines for populations with a long duration of breast-feeding, suggesting that, provided women remained amenorrheic and continued to breast-feed, the method could give good protection for up to 12 months after childbirth irrespective of when supplements are introduced. In this study, the highest 12-month pregnancy rate among the amenorrheic women who were not using contraception was 7.4% (95% CI = 2.5%–12.3%). The range of the CI suggests that although attempts to extend the LAM beyond 6 months in the presence of some degree of supplementation (provided that amenorrhea persists) may be possible, they should be made with caution because more pregnancies can be expected than would be seen with LAM use for only 6 months, as determined in the original Bellagio Consensus (4, 5).

The period of lactational amenorrhea is characterized by a profound degree of protection from pregnancy. Although the suckling stimulus drives the neuroendocrinologic mechanism of lactational infertility, the degree of supplementation to breast-feeding in this study did not yield a dose-response in the pregnancy rate, probably because of the prolonged duration of full breast-feeding in one center that accounted for all the pregnancies that occurred during full breast-feeding in amenorrheic women.

Regardless of the degree of supplementation, the pregnancy rate increased with time from the 6th to the 12th month postpartum. Overall, the rate of pregnancy during amenorrhea was unaffected by variations in the definition of the return of menses. This large, multicenter study found that the cumulative 6-month rate of pregnancy during lactational amenorrhea was between 0.8% (95% CI = 0.1%–1.4%) and 1.2% (95% CI = 0%–2.4%). This is equivalent to the protection provided by many nonpermanent contraceptive methods as they are actually used and upholds the 1988 Bellagio Consensus.

Acknowledgments: Funding for 1 year for the center in Santiago, Chile was provided by the Institute for Reproductive Health, Georgetown University, Washington, DC. The United Nations Development Programme/United Nations Population Fund/World Health Organization/World Bank Special Programme of Research, Development and Research Training in Human Reproduction sincerely thanks the 4,118 mothers and their infants who took part in this study.

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APPENDIX A

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