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Prolonged use of oral contraception before a planned pregnancy is associated with a decreased risk of delayed conception

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BACKGROUND: The aim of this study was to investigate the association of total duration of oral contraceptive usage with time to conception. METHODS: This was a prospective study of 8497 planned pregnancies drawn from a population that recruited 85% of eligible couples in South-West England who were expecting a baby in a 21 month period. Self-completion questionnaires were administered at 18 weeks gestation to ascertain parity, paternity, co-habitation, use of the contraceptive pill, smoking and alcohol status, educational achievement, height, weight and time taken to conceive. Logistic regression was used to identify factors independently related to conception in ≤12 months. RESULTS: Of the participants, 74% conceived in ≤6 months, 14% in 6–12 months and 12% after 1 year. Previous prolonged oral contraceptive usage was statistically significantly associated with a decreased risk of delayed conception. Prolonged use of oral contraception was also associated with improved fecundity independent of other factors. Selection bias due to particularly fertile women using oral contraceptives is unlikely because similar odds ratios were calculated for nulligravid women. CONCLUSIONS: Women who have prolonged use of oral contraceptives might be reassured that they will not be disadvantaged in terms of time taken to achieve conception.

Key words: epidemiology/fecundity/fertility/oral contraception/time to conception

Introduction

The time taken to conceive is a useful epidemiological measure of fecundity (Baird *et al.*, 1986; Joffe, 1997). Approximately 90% of fertile couples conceive within 12 months of trying (Tietze, 1956, 1968; Tuntiseranee *et al.*, 1998a) and a delay of >12 months is therefore usually taken to define infertility or subfertility for clinical purposes (Spira, 1986).

Concern regarding possible impaired fertility after oral contraceptive use has grown during the last two decades and temporary delays in conception compared with other methods of contraception have been reported (Vessey *et al.*, 1978; Linn *et al.*, 1982; Harlap and Barlas, 1984; Chasan-Taber *et al.*, 1997). Influencing factors have included parity and age, with nulliparous women using oral contraceptives until >30 years old reported to have a greater reduction in fertility (Vessey *et al.*, 1986). On the other hand, a study of Thai women found return to fertility after 'pill use' was quicker in nulligravid women compared with multigravid women (Pardthaisong and Gray, 1981). The incidence of post-pill amenorrhoea of ⩾6 months duration was <1% and not related to duration of use or type of pill (Huggins and Cullins, 1990). Women with amenorrhoea following oral contraceptive use were historically and endocrinologically indistinguishable from those who were never users (Hull *et al.*, 1981; Weisberg, 1982). Oral contraceptive users experienced significantly less primary infertility (Bagwell *et al.*, 1995) or tubal infertility caused by infection (Gayer and Henry-Suchet, 1990) than never users. By contrast, past use of intrauterine devices was associated with an increased risk of tubal infertility (Stillman and Berger, 1985; Cramer *et al.*, 1990).

Life-style risk factors affecting primary infertility and corroborated in two or more studies include the use of intrauterine devices and smoking (Buck *et al.*, 1997). Other factors identified include extremes in body size, physical exercise, consumption of alcoholic and caffeinated beverages and use of recreational drugs. Occupational factors have also been identified including manual rather than non-manual occupations, some occupational pollutants (Smith *et al.*, 1997), shift work (Bisanti *et al.*, 1996) and long working hours for

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both the woman and her partner (Tuntiseranee *et al.*, 1998b). The age of the woman has been consistently found to affect fecundity (Schwartz and Mayaux, 1982; Menken *et al.*, 1986) while studies of the man's age have produced conflicting findings (Goldman and Montgomery, 1989; Silber, 1991; van Noord-Zaadstra *et al.*, 1991; Wittmaack and Shapiro, 1992; Ford *et al.*, 2000). All these factors need to be taken into account in assessing the impact of contraceptive usage.

Study methods of fertility have ranged from comparisons of infertile couples with controls, to pregnancy rates by donor insemination treatment in women presumed healthy in terms of fertility, and to general population studies. Although the best method of studying fertility is by observing couples prospectively from the time they start trying to conceive, such studies tend to be small because of practical difficulties (Bonde *et al.*, 1998). Here we have studied the impact of oral contraceptive use on time to conception in a large group of pregnancies that provided sufficient statistical power to allow us to account for other factors that influence fecundity.

Materials and methods

The aim of the Avon Longitudinal Study of Parents and Children (ALSPAC) is to define those environmental and genetic factors that influence the outcome of pregnancy and the health and development of children (Golding *et al.*, 2001). Eligibility criteria were an expected date of delivery between April 1, 1991 and December 31, 1992 and residence in a defined geographical area of Avon in South-West England including a large city and its surrounding small towns and rural area. Women were invited to take part early in pregnancy and an estimated 85% of the eligible population enrolled. The study is by definition a prospective study of fertile couples for birth outcome but retrospective for the time taken to conceive the index pregnancy.

The data in this analysis were derived from separate questionnaires completed by each mother and her partner at 18 weeks gestation. Specific fertility factors included details of previous obstetric and gynaecological history, use of oral contraception and total duration of usage, paternity, whether the pregnancy had been planned, length of time to achieve conception in four bands ($\leq$6 months; $>$6 but $\leq$12 months; $>$12 months but $<$3 years and $\geq$3 years) and duration of current co-habitation. Questions asked about contraception were limited to the use of oral contraceptives; no information was collected on other methods. Information obtained about health, social and demographic factors in the peri-conception period included the woman's body mass index (BMI), level of cigarette smoking and alcohol consumption, her partner's smoking and alcohol consumption, and the woman's environmental exposure to tobacco smoke either at home or at work. The ages of both parents at conception, their ethnic origin, highest educational levels (five point scale), employment at conception, home ownership status, housing type and crowding at home (persons/room) were also obtained.

The measure of fertility used in the present study was time to conception to achieve a pregnancy that reached 24 weeks gestation, i.e. viability. Subfertility was defined as taking at least 12 months to conceive. Excluded from analysis were those who miscarried, those where the mother was $<$16 years of age and those where the partner was reported as not the father of the child. Women had been asked whether their pregnancy was intentional. Of those who replied that this was the case, a further question asked how long it had taken them to conceive. Although a number of women whose pregnancies were unintended did answer the question on length of time to conception, this information is considered unreliable and was not analysed.

Logistic regression analyses identified factors associated with conception within 12 months of the current pregnancy. To address the potential bias of self-selection by women who knew themselves to be particularly fertile, further analysis of conception rates was conducted separately on women who had never been previously pregnant. For analyses of continuous variables, parental age and BMI, quadratic and cubic terms were also offered to the regression analyses. The statistical packages used were Statistics Package for the Social Sciences (SPSS Inc., Chicago, USA) for χ^2-tests and Biomedical Statistics Package (BMDP Statistical Software Inc., Los Angeles, CA, USA) for logistic regression. Statistical significance was indicated by $P < 0.05$.

Results

An estimated 85% of those eligible to take part in the project within the defined geographic area were recruited and numbered 14 893 pregnancies resulting in 14 210 live births. For this analysis there were 12 106 couples initially eligible for study of whom 8497 (70.6%) had conceived intentionally, 3545 (29.4%) had conceived accidentally and only 64 ($<$1%) did not reply to that question. Of those whose pregnancy was planned, 99.5% stated the time taken to conceive: 74.2% within the first 6 months, 13.9% within the second 6 months, 8.5% in the years 2 and 3, and 3.4% after 3 years. The mean age of the women and men at conception was 28 and 31 years respectively; the mean BMI of the mothers before conception was 23 kg/m^2.

Table I indicates duration of oral contraceptive use amongst those who had planned their pregnancies and conceived within 12 months. Increasing duration of oral contraceptive use is statistically significantly associated with an increased proportion of conceptions within 12 months. Table II shows pregnancy intent in relation to duration of oral contraceptive use and indicates that duration of use is highly significant, whether the pregnancy was planned or unplanned. Women reporting that their pregnancy was planned were more likely to have reported longer use of oral contraception. Women who reported an unplanned pregnancy were less likely to have reported longer oral contraceptive use.

Table III shows the duration of oral contraceptive use and various sociodemographic and lifestyle variables. Increasing duration of oral contraceptive use (from $<$1 year to $\geq$5 years) was statistically significantly associated with absence of previous pregnancy or birth, greater ages and education of both partners and duration of co-habitation, higher status housing, greater intake of alcohol for both partners, less smoking by the woman and a higher BMI.

Factors found to be statistically significantly related to delayed conception in this study include older age of both the man and the woman (Ford *et al.*, 2000), the woman's greater exposure to cigarette smoke (Hull *et al.*, 2000), lower level of education and extremes of BMI. There were no significant associations with the ethnic origin of either partner, housing tenure, or maternal alcohol consumption. There was a relatively weak but still significant association between the man's alcohol consumption and conception beyond 12 months. (Unadjusted

Table I. Percentages of conceptions within 12 months of those who stated that their pregnancies were planned in relation to duration of previous oral contraceptive use

	Total (*n*)	Duration of oral contraceptive use					χ^2 (*P*-value)	χ^2 for trend (*P*-value)
		⩾5 years (%) (56.8%)	3–4 years (%) (20.3%)	1–2 years (%) (11.0%)	< 1 year (%) (7.0%)	Never (%) (4.9%)		
No. conceived in 12 months (%)	7139 (88.1)	4122 (89.5)	1444 (88.0)	761 (85.2)	474 (83.5)	338 (85.4)	30.7 (< 0.0001)	26.9 (< 0.0001)

Table II. Pregnancy intent (planned or unplanned) by duration of oral contraceptive use (no exclusions made)

	Total (*n*)	Duration of oral contraceptive use					χ^2 (*P*-value)	χ^2 for trend (*P*-value
		⩾5 years (55.0%) *n* = 6215	3–4 years (22.3%) *n* = 2519	1–2 years (13.3%) *n* = 1504	<1 year (9.4%) *n* = 1062	Never (6.2%) *n* = 744		
Pregnancy intent (%)								
Yes	8497 (70.6)	4779 (76.9)	1716 (68.1)	962 (64.0)	617 (58.1)	425 (57.1)	302.85	232.52
No	3545 (29.4)	1436 (23.1)	803 (31.9)	542 (36.0)	445 (41.9)	319 (42.9)	(< 0.0001)	(< 0.0001)

characteristics with respect to time to conception are not shown but are available from the authors.)

Stepwise logistic regression analyses offered all the variables that were statistically significantly related to conception within 12 months to the model. The longest duration of oral contraceptive usage (⩾5 years) has been preferred for the reference group because of the small size of the never and short-term user groups. Table IV shows adjusted odds ratios (ORs) for achieving conception within 12 months according to the duration of oral contraceptive use for all women in the analysis. A statistically significant association was found between odds of conception within 12 months and duration of previous oral contraceptive use with greatest odds after ⩾5 years use.

For the subset of women who had been previously pregnant ($n = 4254$), Table V shows adjusted ORs for years of oral contraceptive use indicating a statistically significant association between time to conception and duration of use. A similar analysis for the 2133 women who had not been previously pregnant showed there was also a statistically significant difference in terms of time to conception in those who had taken the oral contraceptive pill for >5 years. Using ⩾5 years as the reference group (1.00), the OR for those with <5 years of oral contraceptive use was 0.40 [confidence interval (CI) 0.30–0.52] and for never use the OR was 0.60 (CI 0.31–1.17) (data not shown).

Discussion

This study has shown that among fertile couples, prolonged use of oral contraception is associated with greater subsequent fecundity and the association is strongest after ⩾5 years of usage. This geographically representative study had information on time to conception from early in pregnancy, allowing for a more comprehensive assessment of the many risk factors (personal, social and environmental) compared with many previous studies.

The overall rates of conception are consistent with others reported for fertile populations (Tietze, 1956, 1968) and the factors found to be significantly associated with the chance of conception are consistent with other reports using different study methods.

Age and duration of previous co-habitation are associated with reduced fecundity and both are likely to be associated with prolonged contraception. Those and other factors were controlled for in the adjusted analysis and the independent effects of oral contraceptive usage with increasing duration of use are thus seen to exert a substantial effect on fertility in this population of fertile women. The same was found in a subgroup of women who had never been previously pregnant, thus reducing bias of selective use of oral contraceptives by women who knew they were fertile.

Use of oral contraceptives and subsequent fertility has not been extensively studied, but most studies have reported decreased fertility only immediately after stopping usage. Bracken *et al.* reported on conception delay after oral contraceptive use (Bracken *et al.*, 1990). Their study only included women married to their first partner who had conceived within 24 months. Their sample was more likely to be younger, non-white, smokers, primagravida, less educated and non-drinkers, considerably different from the women in our study. Information on length of time using oral contraceptives was not available from the Bracken *et al.* study. However, they did differentiate between high and low estrogen oral contraceptives, reporting that high estrogen contraceptives had a greater negative effect on return to fertility (Bracken *et al.*, 1990). This is important for the interpretation of our present study performed in the 1990s, when the majority of women used low dosage estrogen pills.

Study results from a large cohort of nurses indicate that

Table III. Duration of oral contraceptive use and sociodemographic and lifestyle variables. All values are percentages unless otherwise specified

	⩾5 years (56.8%)	3–4 years (20.3%)	1–2 years (11.0%)	<1 year (7.0%)	Never (4.9%)	χ^2 (*P*-value)
Previous pregnancies (n = 8098)						
None (31.9)	61.2	18.4	9.3	6.2	4.9	30.99
⩾1 (68.1)	54.9	21.0	11.8	7.4	4.9	(< 0.0001)
Previous children (n = 7915)						
None (44.0)	59.3	19.1	9.9	6.8	4.9	14.06
⩾1 (56.0)	55.5	20.8	11.8	7.1	4.8	(< 0.01)
Years of co-habitation (n = 7569)						
0, 1 (8.4%)	44.4	21.4	16.5	11.5	6.1	
2, 3 (24.7)	50.6	24.4	12.5	7.6	4.9	
4, 5 (27.6)	58.3	21.5	10.5	5.5	4.1	
6, 7 (18.0)	64.7	16.9	8.9	5.9	3.6	
8, 9 (10.4)	66.9	17.0	7.3	5.3	3.4	
10, 11 (6.3)	67.4	15.2	7.2	4.6	5.7	
12, 13 (2.5)	63.0	16.1	8.9	4.7	7.3	216.25
⩾14 (1.9)	59.2	16.2	7.7	5.6	11.3	(<0.0001)
Woman's age (n = 8144)						
<19 (1.8)	2.0	16.3	37.4	32.7	11.6	
20–24 (16.5)	35.2	31.1	18.4	10.1	5.2	
25–29 (43.2)	61.9	20.3	9.0	5.1	3.7	
30–34 (29.5)	63.8	15.8	8.9	6.5	5.0	734.97
⩾35 (9.0)	60.3	15.4	8.8	7.3	8.2	(< 0.0001)
Man's age (n = 7875)						
<19 (11.2)	37.1	22.8	19.3	13.1	7.7	
20–24 (33.0)	56.7	21.9	11.0	6.7	3.7	
25–29 (34.6)	60.9	19.7	9.5	5.9	4.0	
30–34 (14.2)	62.1	17.2	8.6	5.7	6.3	252.67
⩾35 (7.0)	57.5	17.6	10.5	7.0	7.4	(< 0.0001)
Woman's ethnicity (n = 7847)						
White (97.4)	57.7	20.4	10.7	6.8	4.4	86.69
Non-white (2.6)	37.1	13.3	18.9	12.6	18.2	(< 0.0001)
Man's ethnicity (n = 7819)						
White (98.2)	57.6	0.4	10.8	6.8	4.5	31.88
Non-white (1.8)	48.7	15.1	14.6	10.1	11.6	(< 0.0001)
Woman's education (n = 7886)						
CSE or less (16.5)	50.0	21.2	12.3	10.6	5.9	
Vocational (9.6)	57.3	20.2	12.4	6.5	3.6	
O level (35.2)	60.2	21.0	9.9	5.4	3.5	
A level (24.0)	58.7	20.0	9.9	6.7	4.6	94.32
Degree (14.7)	55.9	18.1	12.2	6.9	7.0	(< 0.0001)
Man's education (n = 7708)						
CSE or less (22.1)	54.5	20.8	12.2	8.2	4.4	
Vocational (8.4)	54.0	24.0	8.8	8.7	4.5	
O level (21.5)	59.6	19.9	10.4	5.8	4.2	
A level (27.8)	61.3	19.5	9.7	5.2	4.4	57.45
Degree (20.2)	54.9	19.4	11.8	7.8	6.1	(< 0.0001)
Housing type (n = 8046)						
Detached (16.0)	62.2	18.0	9.1	5.6	5.2	
Semi-det. (36.2)	59.7	20.1	9.6	6.1	4.5	
Terraced (33.2)	58.0	20.5	10.7	6.2	4.6	177.76
Flat/other (14.6)	42.2	22.0	17.1	12.8	5.8	(< 0.0001)
Housing tenure (n = 8060)						
Owned/mortgaged (81.5)	61.0	19.3	9.5	5.6	4.52	
Council (10.1)	37.4	26.8	18.0	12.9	4.8	96.07
Rented/other (8.4)	42.1	20.3	16.7	13.0	7.9	(< 0.0001)
Overcrowding (n = 7990)						
No (96.1)	58.1	20.3	10.7	6.4	4.5	139.13
Yes (3.9)	32.3	20.1	18.2	18.2	11.2	(< 0.0001)
Woman smoked (n = 8144)						
Yes (26.5)	55.9	20.3	12.2	8.1	3.5	22.44
No (73.5)	57.2	20.2	10.6	6.6	5.4	(< 0.001)
No. cigarettes woman smoked (n = 8073)						
None (73.5)	57.2	20.2	10.6	6.6	5.4	
1–9/day (7.8)	59.4	18.6	10.0	8.2	3.8	
10–14/day (5.4)	54.3	23.2	10.8	9.2	2.5	
15–19/day (5.9)	50.5	23.2	14.7	9.5	2.1	48.22
⩾20/day (7.3)	56.2	19.1	13.5	7.2	4.0	(< 0.0001)

Table III. *continued*

	⩾5 years (56.8%)	*3–4 years* (20.3%)	*1–2 years* (11.0%)	*<1 year* (7.0%)	*Never* (4.9%)	χ^2 (*P*-value)
Woman's exposure to smoke (n = 8105)						
None (49.3)	57.4	20.1	10.4	6.6	5.5	
Passive only (23.9)	57.4	20.0	10.9	6.7	5.1	
Mother smokes only (7.6)	60.9	19.3	10.6	6.8	2.3	29.02
Mother smokes and passive (19.2)	54.6	20.7	12.5	8.4	3.7	(< 0.01)
Man smoked (n = 7954)						
Yes (30.1)	56.7	19.7	11.8	7.5	4.3	6.68
No (69.1)	57.3	20.3	10.6	6.7	5.1	NS
No. cigarettes partner smoked (n = 7758)						
None (69.1)	57.3	20.3	10.6	6.7	5.4	
1–9/day (9.3)	59.4	19.4	11.7	4.9	4.5	
10–14/day (5.3)	53.9	20.3	10.8	9.6	5.4	
15–19/day (5.9)	56.4	19.9	11.7	8.8	3.1	25.56
⩾20/day (10.5)	55.0	19.7	13.1	8.3	4.0	NS
Woman's alcohol consumption (n = 8119)						
None (7.0)	35.4	23.7	14.9	16.5	9.5	
<1 glass/day (82.6)	57.4	20.4	11.0	6.5	4.7	194.33
⩾1 glass/day (10.4)	66.9	16.3	9.0	4.7	3.1	(< 0.0001)
Man's alcohol consumption (n = 8057)						
None (3.9)	35.9	22.3	14.6	14.9	12.3	
<1 glass/day (78.1)	56.2	20.7	11.2	7.1	4.8	139.75
⩾1 glass/day (18.0)	65.3	18.3	8.4	4.6	3.4	(< 0.0001)
Woman's BMI (n = 8144)						
0–10th centile (15.1)	48.1	22.4	13.2	9.0	7.3	
10–20th centile (9.8)	54.8	21.0	10.7	8.2	5.3	
20–40th centile (18.9)	58.7	19.9	9.4	7.2	4.8	
40–60th centile (18.6)	60.3	18.0	11.0	6.3	4.3	
60–80th centile (18.8)	60.7	20.8	9.3	5.7	3.6	
80–90th centile (9.5)	60.8	18.9	10.4	5.3	4.5	105.76
90–100th centile (9.3)	50.3	21.3	15.4	7.9	5.0	(< 0.0001)

BMI = body mass index; NS = not significant

Table IV. The effect of the duration of oral contraceptive use on the odds ratios (95% confidence intervals) for achieving conception within 12 months for all women in the study. Adjustment was made for woman's and man's age at starting to try to conceive (+ quadratic term for woman's age), woman's body mass index (+ quadratic term), education, exposure to smoking, parity, housing type and years of co-habitation

	⩾5 years (ref.)	3–4 years	1–2 years	<1 year	Never	χ^2 (*P*-value)
Years of oral contraceptive use	3849 (59.1%)	1311 (20.1%)	678 (10.3%)	407 (6.2%)	279 (4.3%)	
Conception within 12 months (n = 5754; 88.2%)	1.00	0.71 (0.56–0.91)	0.52 (0.39–0.70)	0.46 (0.33–0.65)	0.67 (0.43–1.06)	33.24 (< 0.0001)

Table V. The effect of the duration of contraceptive usage on the odds ratios (95% confidence intervals) for achieving conception within 12 months for women who had been pregnant previously (n = 4254). Adjustment was made for woman's and man's age at starting trying to conceive (+ quadratic term for woman's age), woman's BMI (+ quadratic term), education, exposure to smoking, housing type and years of co-habitation

	⩾5 years (Ref)	<5 years	Never	χ^2 (*P*-value)
Years of oral contraceptive use (n = 4254)	2415 (56.8%)	1653 (38.9%)	186 (4.3%)	35.45
Conception within 12 months (n = 3811; 89.6%)	1.00	0.83 (0.63–1.09)	0.61 (0.44–0.85)	(< 0.0001)

fertility is reduced briefly but returns to normal within 3 months with no significant subsequent delay to conception for 'ever users' and no increasing risk of infertility with increasing duration of use (Chasan-Taber *et al.*, 1997). However, our present analysis found increased fertility related to prolonged usage of oral contraception, particularly for ⩾5 years. This was also the case in women who had never been pregnant before. Other studies do not appear to have collected or analysed data for oral contraceptive use of ⩾3 years.

Information on time taken to conceive was retrospective but collection was early in pregnancy and recollection of time taken to conceive has been found to be reliable (Joffe, 1997). Reporting bias for information related to fertility was likely to have been avoided, as couples were aware only of the research interest in the pregnancy and the health of the developing child. The study of fertile couples minimized effects due to definable causes of subfertility and relative reproductive ageing. However, fecundity varies greatly within the normal population: from a peak birth rate of ~30% in the first cycle, it falls exponentially to 5% each cycle after a year, with a median of ~20% (Spira, 1986). Our study population exhibited the same pattern, consistent with other birth rate studies (Vessey *et al.*, 1978; Tuntiseranee *et al.*, 1998a); the monthly rates approximately halving after 6 months and halving again after 12 months. Thus the measure of time to conception provided a sensitive index to assess factors affecting relative fecundity. The study of other similarly fertile populations may result in different findings.

Time to pregnancy in this study was recorded in ordinal categories rather than as a continuous variable. The latter would have allowed more powerful statistical analysis and possible recognition of the initial reduction of fecundity after stopping oral contraception. However, in practice longer delay to conception is of greater importance and our analysis revealed a significant benefit of oral contraceptive usage to achieve conception subsequently within 12 months. Any initial reduction in fecundity may be at least partly behavioural, due to advised delay before attempting to conceive (Spira *et al.*, 1985). A reduction in fertility in the first months after stopping oral contraceptive use might also be explained by the delay of the body in returning to normal ovulation.

Whilst possible selection bias for use of oral contraception by relatively fertile women was excluded by demonstration of the same beneficial effects on women who had never been pregnant before, it was not possible to compare oral contraception with other methods. Most recently Doll *et al.* have reported on return to fertility in nulliparous women after discontinuation of the intrauterine device (Doll *et al.*, 2001). Their research compared methods of contraception and although no association was found between fertility and duration of oral contraceptive use, there were only 158 oral contraceptive users included in the study.

Our study questionnaire did not distinguish between estrogen/progestogen and progestogen-only pills, but it is known that in the UK at the time the data were collected the combined preparation accounted for 95% of oral contraceptive users aged 20–29 years (Thorogood and Vessey, 1990). Use of the progestogen-only pill has no reported association with delayed conception (Weisberg, 1982).

There remains the question of whether all appropriate confounders and risk factors were taken into account (Basso *et al.*, 1997). Information as to coital frequency was not available and, while an important determinant for the chance of conception, it is known to vary with time and through the ovulatory cycle. However, discontinuation of oral contraception to achieve pregnancy after prolonged use might have been accompanied by more frequent or more appropriately timed coitus.

The greater chance of conception associated with prolonged oral contraceptive usage is likely to represent an increasing advantage rather than a decreasing disadvantage. A possible explanation could be a protective effect by minimizing endometrial proliferation and menstrual shedding, preventing damaging progression of endometriosis (Vercellini *et al.*, 1993a,b; Vessey *et al.*, 1993). The same effect may also prevent progressive endometrial dysfunction that might develop with prolonged cyclical proliferation. There is evidence that women who lack endometrial development due to estrogen deficiency as a result of ovarian failure are subsequently more receptive to implantation of (donated) oocytes than menstruating women (Edwards, 1992).

Other mechanisms that may benefit fertility and explain the effect of long-term oral contraceptive use include improved iron stores. A Danish study of iron status in pre- and postmenopausal women showed that the number of years taking the contraceptive pill was positively correlated with serum ferritin (Milman *et al.*, 1993). Evidence from an Australian prospective study of pregnancy, also confined to women who had given birth, indicated that long-term oral contraceptive use was associated with a reduced risk of age-related miscarriage (Ford and MacCormac, 1995). Women who conceive within 3 months after stopping oral contraception also have an intrinsically lower risk of a chromosomally normal spontaneous abortion. Rates of spontaneous abortion in previous pregnancies were also lowest in women who had conceived quickly after stopping the pill (Sackoff *et al.*, 1994). Ford and MacCormac have also suggested that oral contraceptives protect against age-related miscarriage, mainly due to trisomy, by suppression of ovulation and therefore preservation of the number of follicles (Ford and MacCormac, 1995). Rat studies of long-term exposure to GnRH antagonists have shown significant preservation of follicles. There is also evidence that age-related trisomy is associated with decline in numbers of follicles independent of age (Brook *et al.*, 1984; Faddy *et al.*, 1992; Meredith *et al.*, 1992). Follicular preservation by oral contraception would be expected to delay the menopause (Stanford *et al.*, 1987). Women who began oral contraceptive use in the mid 1960s are only now reaching the age of menopause (Cramer *et al.*, 1995; Ford and MacCormac, 1995) so it may yet be too early to observe. However, animal studies and modelling of observed human data suggest that falling oocyte number is only weakly associated with ovarian failure (Thomford *et al.*, 1987).

It has also been suggested that women in prehistoric times may have had far fewer periods than modern women, a later menarche (~16 years of age), earlier first births (19.5 years), frequent pregnancies and long duration of breastfeeding (Thomas and Ellertson, 2000). Whether current menstrual patterns have health benefits is unknown, but there is some evidence that amenorrhoea is often healthier than the alternative (Coutinho, 1999).

In conclusion, we found in a large population of couples having a baby, previous prolonged use of oral contraception was associated with improved fecundity independent of other

factors. Although increasing benefit with greater duration of usage would be consistent with any of the possible protective mechanisms above, selection bias may have been introduced due to our inability to compare oral contraceptive use with other methods of contraception. In the UK, 25% of women between the ages 16–49 years use the pill as a method of contraception (Department of Health UK, 1997) and while women who have prolonged use of oral contraceptives might be reassured that they will not be disadvantaged in terms of the time they are likely to take to conceive, study of other populations may result in different findings.

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