



Acta Genet Med Gemellol 34:105-108 (1985)
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Received 5 June 1984
Final 10 September 1984

A Study of the Influence of Ovulation Stimulants and Oral Contraception on Twin Births in England

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Abstract. A study of 111 mothers of twins in Nottinghamshire, England, in 1981-82 showed that at least 12 had used ovulation stimulants, compared to 2 of 102 mothers of singletons. Thus, the use of ovulation stimulants increased the twinning rate of this population by about 10 percent; this may explain the recently noted levelling off in the secular decline in twinning rates. In contrast to a recent study in France, no association between twinning and prior use of oral contraceptives was seen.

Key words: *Twinning rates, Ovulation stimulants, Oral contraceptives*

Although the increased risk of twinning following the use of ovulation stimulants is well recognised [1], the proportion of twin births caused by these drugs has rarely been estimated, and the effect on secular trends in twinning rates has not been assessed. In a large French study, 11.4% of twin birth followed the use of such drugs [2]. The same study showed that mothers who had used oral contraceptives prior to the pregnancy had a much reduced risk of twinning, with a relative risk compared to mothers using other sorts of contraception or no method of 0.75.

We performed a case control study of twin births in Nottinghamshire, England, to assess these two points. A postal questionnaire was sent to all mothers (145) resident in Nottinghamshire who gave birth to legitimate live born twins between January 1981 and August 1982, and to mothers of each next registered legitimate live singleton birth. For mothers over 35, two comparison mothers were selected for each mother of twins, giving in total 160 comparison mothers. Replies were obtained from 111 mothers of twins and 102 mothers of singletons. The mothers of twins reported a personal or family history of twinning more often than the comparison mothers, but adjustment for this difference did not affect the results reported here. The two groups did not differ substantially in age, parity, social class, height or obesity.

Of the mothers of singletons, five had sought medical treatment for infertility and two of these had received ovulation stimulants (Table). Of the mothers of twins, twelve had received ovulation stimulants, while four others reported being treated for infertility without specifying the method and so may have received such drugs. Thus at least 10.8%, and up to 14.4%, of twin births followed the use of such drugs. The relative risk of twinning in the mothers who used ovulation stimulants, compared to those with no history of infertility, was 6.3 (95% confidence limits 1.6, 24.2). The relative risk for the occurrence of like sex pairs was, as expected, lower than that for unlike sex pairs (4.6 vs 12.8) although the difference was not significant.

After exclusion of mothers who had sought treatment for infertility, mothers of singletons and mothers of twins were compared in regard to the method of contraception used prior to the index birth; no significant differences were seen. Comparing oral contraceptive users with all other mothers gave a relative risk for twinning of 1.1 (95% confidence limits 0.6, 1.9). For unlike sex pairs, the relative risk is 2.3, but with wide limits of 0.8 and 6.4. For the mothers who had used oral contraception, we examined the total duration of use of oral contraception, and also the time interval since stopping oral contraception. There was a trend for the risk of twinning to rise with increasing duration of oral contraceptive use, although this did not quite reach significance, while there was no association seen with the interval since stopping use. Five of the singleton pregnancies and seven of the twin pregnancies were reported to have occurred "accidentally" while the mother was still using oral contraception.

Comment

This small study suggest that about 11% to 14% of twin births follow the use of ovulation stimulants. This is similar to the estimate of 11.6% in a larger study in France [2]. Taking into account the small number of singleton pregnancies following such births, the use of these drugs therefore appears to increase the background "natural" twinning rate by about 10%. The fact that twinning rates in most Western countries, including England and Wales, have fallen dramatically since the 1950s has received considerable attention [3], and we have recently noted that this fall in twinning rates has apparently levelled out in the 1970s [4]. However, a comparison of the trend up to 1970 with this estimated "natural" twinning rate being 10% below the recorded twinning rate in recent years, suggests that the trend in natural twinning rate has continued to decline, and the apparent levelling off in the observed twinning rate may be due to the proportion of twin births caused by the use of ovulation stimulants (Figure).

The French study showed a significant reduction in the probability of twinning in mothers who had previously used oral contraceptives. We found no evidence for such a decrease, although, because our study is small, the results of the two studies combined still show a statistically significant reduction of twinning in oral contraceptive users. The study populations are very different; in the French study, 38% of mothers of singletons reported using no contraception and 9% reported using barrier or other methods, whereas in our study the corresponding proportions are 16% and 36%. In the French study, mothers who had used barrier methods had the highest frequency of twinning, whereas in our study they had the lowest. The complex array of factors which affect the choice of contraceptive method makes the interpretation of relationships between contraceptive usage and twinning difficult, and our failure to confirm the observation first made in France suggests that further work is required.

Table. Prior Use of Ovulation Stimulants and Methods of Contraception in Mothers of Twins and of Singletons, Nottinghamshire, 1981-1982

Total number	Singletons (N = 102)	All twins (N = 111)	Like-sex pairs (N = 87)	Unlike-sex pairs (N = 24)
History of infertility:				
Ovulation stimulants used	2	12	7	5
Other treatment used	3	2	7	0
Treatment method unknown	0	4	4	0
No history of infertility	97	93	74	19
Last method of contraception:				
None	15	18	18	0
IUD, barrier, other	35	28	22	6
Oral	47	47	34	13

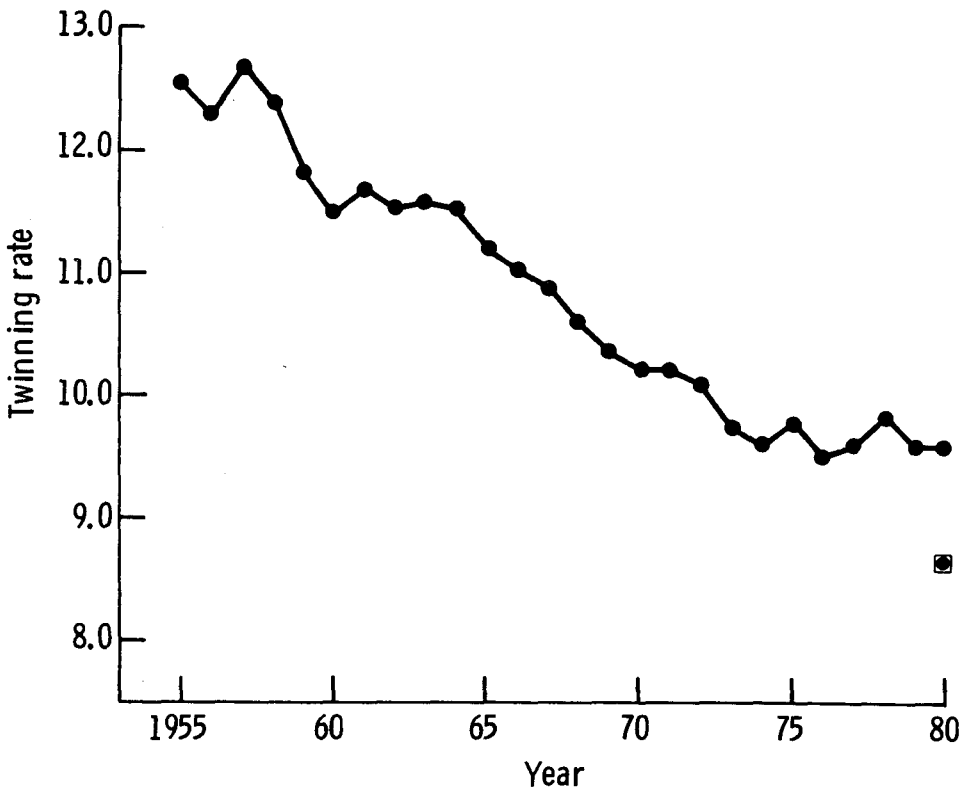


Figure. Total twinning rate (twin pairs per 1,000 maternities) by year, 1955 to 1980, England and Wales, and estimated twinning rate, 1980, after exclusion of births associated with ovulation stimulants.

We thank the records staff of the Nottingham District Health Authority for their assistance.

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