

might wonder whether the pill *does* have the effect Bracken suggested.

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Reply to Dr. James

To the Editors:

In his early British study Bulmer¹ found that the rate of twins conceived in the first 3 months of marriage exceeded expectation by 19% and a 7% higher twinning rate was found for twins conceived before marriage. Australian data² (1944 to 1963) show that the rate of twins delivered in the first 12 months of marriage was 9% higher than the rate of twins delivered between 13 and 24 months of marriage. One reasonable hypothesis from these observations is that more fecund women are both more likely to conceive when unprotected coitus first occurs and more likely to conceive twins. Since the available studies concern married women, however, other explanations for these findings must also be entertained. To state that these observations are "well established" prematurely closes an issue still under debate. The reported fecundity effects moreover are quite small and would be unlikely to account for the 100% increased general twinning rate following recent oral contraceptive (OC) exposure observed in our study.³

Dizygous twinning has declined in some countries but these trends started long before widespread OC use. From Dr. James' own data⁴ we have computed an overall (unweighted) decline of 11% between 1957 and 1961 and 1967 and 1969 in England and Wales. The reasons for this decline are not clear but they do not conflict with the finding that recent OC exposure at least doubles the twinning rate. In our study 10.4% of all women delivering were exposed to OCs 2 months or less before conception. This frequency of exposure would actually require a 67% national decline in dizygous twinning to entirely negate the threefold increased risk of dizygous twinning found in our study for women recently exposed to OCs.

In response to Dr. James' letter we analyzed our data for twinning rates after recent discontinuation of other forms of contraception. In all, 27.5% of women delivering were exposed to other contraceptives (diaphragm, jelly, cream, foam, intrauterine contraceptive device, rhythm, condoms, withdrawal, or douche) less than 3 months before conception. The twinning rate in these

women was 1.4% versus 1.7% in women not exposed (Fisher's exact one-tailed *p* value = 0.34; odds ratio = 0.84). The twinning rate for recent exposure to other contraceptives, therefore, is less than half that of the 2.9% found for recent exposure to OCs³ and is not significantly different from that for women who had not practiced contraception for 3 or more months prior to conception. A number of women were exposed to both OCs and other forms of contraception within 3 months of conception. Adjusting for this multiple exposure in a log-linear model did not change the initial findings ($\Delta G^2 = 0.32$).

This analysis further supports the hypothesis that increased twinning following recent OC exposure is indeed peculiar to prior use of OCs rather than to a general fecundity effect in all sexually active women recently exposed to conception. The biological basis for increased dizygous twinning due to increased pituitary gonadotropin release and multiple ovulation following a period of recent suppressed ovulation because of OC usage remains an intuitively more appealing hypothesis.

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Twinning in postpill spontaneous abortions

To the Editors:

Dr. Bracken's interesting article on "Oral contraception and twinning" (AM. J. OBSTET. GYNECOL. **133**:432, 1979) has prompted me to review my spontaneous abortion material from the standpoint of postpill twinning.

From 1976 to mid-1979 I have personally examined 619 spontaneous abortions, of which 446 (72.1%) had enough embryonic/fetal and placental tissue to allow a firm "karyotypic" diagnosis. This indirect method of "karyotyping" abortions, using the gross and microscopic morphology of the abortus, has an overall diagnostic accuracy of 80%,¹ and preliminary results from an ongoing correlative cytogenetic and pathologic study support its validity.² Of the seven twin abortions seen in this series, four were labelled "diploid" and three "trisomic." These "trisomic" abortions (dizygotic with two separate empty chorionic sacs) occurred in

women conceiving within 1 to 5 months of cessation of oral contraceptives. This finding, although based on small numbers, deserves further evaluation and, with the low occurrence of twin spontaneous abortions, it is unlikely that one center could collect enough data for meaningful conclusions re twinning, heteroploidy, and recent pill exposure. I feel that a systematic multicenter investigation is clearly indicated.

There is no agreement on the incidence of heteroploidy in postpill spontaneous abortions,³ and the data relating to twin spontaneous abortions are inadequate.⁴ Correlative clinical, pathologic, and cytogenetic studies on all postpill spontaneous abortions will undoubtedly yield valuable information concerning the pathophysiology of the postpill state and the pathogenesis of heteroploidy in humans.

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Reply to Dr. Honoré

To the Editors:

Dr. Honoré does not say how his case series was collected (for example, were they all consecutive cases?) but the twinning rate of between 1.1% and 1.6%, depending upon which denominator is used, suggests that his rate of twin spontaneous abortions is not dissimilar to the usual rate of twin deliveries. Recent exposure to oral contraceptives in three of the seven mothers of spontaneously aborted twins also generally agrees with that in the mothers of twins delivered at term.¹

I certainly agree that we need to know much more about spontaneous abortion and also about all pregnancy outcomes as well as fertility in general after oral contraceptive use. Such studies should be designed to permit the control of possible confounding maternal factors on pregnancy outcomes. We know from many studies, for example, that women who use oral contraceptives are also significantly more likely to be heavy smokers,² to drink alcohol frequently,³ and to have a history of previous induced abortions.⁴ Preliminary data from our own research indicate that women who

smoke may conceive more rapidly after stopping oral contraception than women who do not smoke. Whether this is a pharmacologic effect or it is due to other characteristics of women who smoke and use the pill is presently unclear.

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Determination of correct karyotype

To the Editors:

With reference to the letter of Dobelle and associates (*AM. J. OBSTET. GYNECOL.* **130**:117, 1978) and the article by Stenchever and Parks (*AM. J. OBSTET. GYNECOL.* **127**:143, 1977) the only way to ensure that karyotyping of chromosomes 8 and 9 is done correctly is to perform

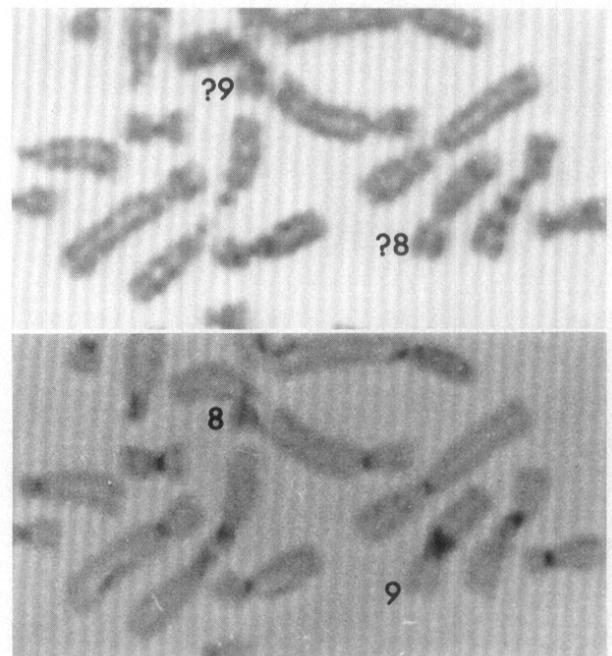


Fig. 1. Identification of chromosomes 8 and 9 by use of G and C banding.