Notes Towards an Epidemiology of Spontaneous Abortion

W. H. JAMES

Department of Psychology, Dalhousie University
Halifax, Nova Scotia, Canada

THIS PAPER will examine data relating to two aspects of the epidemiology of spontaneous abortion. First I shall use a form of analysis (James, 1961) to reassess the statistical evidence for the clinical notion that women segregate into abortion-prone and abortion-resistant groups. Second, I shall consider the relation of maternal age and birth order to spontaneous abortion.

Since the discussion in both sections depends on the thesis that women differ greatly in their propensity to abort (called here their "abortion-probability"), and since this has been recently disputed (Warburton, 1961; Warburton and Fraser, 1959), I shall present fresh evidence on this point. And since the additional fertility following an abortion is a point which will also be raised in both sections, some preliminary observations will also be offered on this topic.

VARIATION BETWEEN WOMEN IN ABORTION-PROBABILITY

Three different lines of argument will be used in this context:

(1) Observed frequencies of women within a gravidity group who have had 0, 1, 2 . . . abortions do not follow binomial expectations;

(2) The variance of the observed distributions is large, yet the results of adjacent pregnancies in an obstetric history do not correlate;

(3) Empirical examination suggests that pregnancies following a series of abortions have a far higher probability of aborting.

The Sample

Warburton (1961) presented a good summary of the types of bias associated with the commoner sources of data on spontaneous abortion. She concluded that the best source is a random sample of women interviewed by a skilled interviewer. Through the courtesy of the Trustees of the Institute for Sex Research of Indiana University, I have been given permission to present and re-analyse some of their previously published data and to analyse previously unpublished data as well. The sample of women from which these data were elicited has been described elsewhere (Gebhard, Pomeroy, Martin and Christenson, 1958, pp. 11-23). The training of the interviewers and the very thorough efforts to gain rapport with the subjects are described by Kinsey, Pomeroy and Martin (1948, ch. 2). Although the representativeness of the sample is admittedly incomplete (Gebhard *et al.*, 1958, pp. 18-23), it seems unlikely to have affected those features of the sample to be reported.

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The sample was of 781 white women, each of whom:

a) was 36 or more years old at the time of interview,
b) had married by the age of 30,
c) had never been to prison,
d) had had at least one pregnancy.

This sample includes the 759 gravidae mentioned on p. 136 of Gebhard *et al.* (1959). The additional 22 women were interviewed after the manuscript for the book had been prepared for publication. I shall call the 781 women the ISR Sample.

TABLE 1. WOMEN IN THE ISR SAMPLE. FREQUENCIES OF WOMEN WITH THE GIVEN COMBINATIONS OF PREGNANCIES AND SPONTANEOUS ABORTIONS

		Spontaneous abortions									
		0	1	2	3	4	5	6	7	8	Total
	1	136	27								163
P	2	214	34	6							254
r	3	98	45	15	5						163
e	4	32	18	17	8	2					77
g	5	8	11	9	3	2	0				33
n	6	4	3	6	4	4	2	0			23
a	7	0	1	1	0	1	2				5
n	8						1				1
c	9	1									1
i	10	1			1		1	1	1		5
e	11							1			1
s	12						1			1	2
											728

The remaining 53 women in the ISR Sample had their every pregnancy terminate in induced abortion.

Table 1 shows the frequencies among these women with the given combinations of pregnancies and spontaneous abortions. In all cases induced abortions (therapeutic or criminal) are ignored; so, for example, a woman reporting one live birth, one spontaneous abortion and one induced abortion is recorded as having had two pregnancies, one of which yielded a live birth and the other a spontaneous abortion. It is here assumed that among those pregnancies which in fact ended in induced abortion, the same proportion would have spontaneously aborted if the pregnancies had not been artificially terminated. (Data on the gestation periods of illegal abortions are not known to this author.)

1. *Testing for Binomial Expectations*

If the probability of aborting a pregnancy were equal in all women and equalled $q = 1-p$, then within a group of k women each of whom has had exactly n pregnancies, the expansion of the binomial $k(p+q)^n$ should give the expected frequencies of women who have had 0, 1, 2, . . .n abortions (this formulation is subject to a condition to be stated later). Table 2 shows the frequencies observed and those expected on the binomial hypothesis for those women with from three to six pregnancies ($p = 1 - q$, the basis of the expected frequencies, was calculated separately for each gravidity group).

TABLE 2. WOMEN IN THE ISR SAMPLE WITH 3, 4, 5 AND 6 PREGNANCIES. FREQUENCIES OF WOMEN OBSERVED AND EXPECTED ON THE DOUBLE BINOMIAL, SKELLAM'S DISTRIBUTION AND THE NEGATIVE BINOMIAL

		Abortions							
		0	1	2	3	4	5	6	Total
3 Pregnancies	O	98	45	15	5				163
	D	98.4	44.0	16.0	4.7				163.1
	B	88.5	59.9	13.5	1.0				163.0
4 Pregnancies	O	32	18	17	8	2			77
	D	31.5	20.6	13.8	8.7	2.4			77.0
	B	21.5	32.3	18.2	4.5	0.4			77.0
	S	30.4	22.2	14.2	7.5	2.7			77.0
	N	28.1	26.2	14.1	5.8	2.0			76.2
5 Pregnancies	O	8	11	9	3	2	0		33
	D	11.5	8.3	5.5	4.6	2.5	0.6		33.0
	B	6.4	12.4	9.6	3.7	0.7	0.1		33.0
	S	8.0	11.1	8.3	4.1	1.3	0.2		33.0
	N	7.7	11.7	8.4	3.7	1.2	0.3		33.0
6 Pregnancies	O	4	3	6	4	4	2	0	23
	D	4.2	3.9	3.9	4.8	4.0	1.8	0.3	23.0
	B	1.3	4.7	7.3	6.1	2.8	0.7	0.1	23.0

O = observed.
D = double binomial.
S = Skellam's distribution.
N = negative binomial.

For the binomials, chi-square = 19.8173 with 4 d.f., $p < 0.001$

Thus the fit is completely unsatisfactory. However, it was just remarked that the binomial frequencies would be expected only if a certain condition were satisfied. The condition is that women do not selectively conclude their reproductive performance according to the 'score' of their obstetric history. I shall later present data which suggest that, in fact, this condition is not satisfied. Women, it will be shown, are more likely to engage in a further pregnancy if the last one aborted than if the last one yielded a live birth. At first sight, it might be argued that it is this fact which frustrates the binomial expectations. However, if there were underlying binomial frequencies which had been disturbed by this selectivity, the effect would be to reduce the frequencies of women with high proportions of aborted pregnancies; there would be fewer women in the tails of the distributions. Yet the observed frequencies of women with 50 per cent or more pregnancies aborting *exceeds* the frequencies expected on the binomial hypothesis. It is concluded that if there are underlying binomial frequencies, it is not this selectivity which has interfered with them.

2. *The Variance of the Observed Distributions*

For the binomial distribution, the mean is np and the variance npq, so it is noteworthy that in three of the four observed distributions (for gravidae 3 to gravidae 6) the variance exceeded the mean. It implies either that the women varied in their abortion probabilities or that there is a positive correlation between the outcomes of successive pregnancies. This latter alternative may be tested by applying a runs test. If there were such a positive correlation, the number of "runs" of similar outcome within each obstetric history would be expected to be smaller than would be predicted on the basis of chance. However, the runs test is not very efficient; for a woman with two abortions it cannot discriminate at the 5 per cent level unless she has had 14 or more pregnancies. And in no case can the test discriminate at the 5 per cent level in a history of less than nine pregnancies. Women in these categories are comparatively rare; even more rare are such women who can remember the *order* of the outcomes of their pregnancies. However, it is possible to combine the results of a number of tests of significance; the composite result may be expressed in terms of a single probability. Fisher (1932) considered the case of k values of a probability $p_1, p_2, \ldots p_k$. He showed that $M^2 = -2 \log_e \prod_{j=1}^{k} p_j$ is distributed as χ^2 with $\nu = 2k$ degrees of freedom.

Swed and Eisenhart (1943) have tabulated the probability of $P\,[u \leqslant u']$ where u' is the observed number of runs in a sequence composed of n objects of one kind and m of another (m and n taking the values of two or more). So for each woman who has had 2+ live births and 2+ abortions (and who remembers the order in which they occurred) a probability may be quoted that the number of runs would be equal to or less than the observed number. From data provided by the Institute for Sex Research it was found that there were 30 white nonprison women whose obstetric histories could be tested in this fashion (The histories of prison women and Negro women were not so tested because it was believed that in the case of women recovering from or contracting syphilis during their reproductive lives, the abortion-probability might fluctuate, thus violating an assumption of the runs test.)

From the data, it was found that $M^2 = 43.761$ with 60 d.f., a value which is clearly not significant. It is concluded that the outcomes of adjacent pregnancies do not correlate and that, therefore, the women varied in their propensity to abort.

3. *Empirical Data on Recurrence Rates*

I have published data elsewhere (James 1962; James 1963) which indicate that a woman who aborted her last two or three pregnancies has a far higher chance of aborting her next pregnancy. Bearing in mind the lack of correlation between the results of adjacent pregnancies, this again suggests that women do, indeed, vary greatly in abortion- probability.

It should be noted that the high variances in the observed distributions suggest that the abortion-probability remained relatively constant within each woman; if it had varied, that would have reduced the variance (Edwards, 1960). Accordingly, it is concluded that abortion probabilities do, in fact, vary from one woman to another, although not appreciably within a given woman. This, of course, is intended only as a generalization, and is not meant to deny that in a few cases abortions are associated with blood group incompatibility, and that the probability of iso-immunization increases with gravidity (Glass, 1949). During the rest of this report, I shall treat this point as if it were established; I shall refer to "abortion-prone" and "abortion-resistant" women, with the implication that women vary (though do not necessarily segregate) in this regard. It is important, therefore, to consider how this probability is distributed.

ADDITIONAL FERTILITY FOLLOWING AN ABORTION

First, it is necessary to examine the consequences of a point already mentioned, the additional fertility contingent upon an abortion. As far as I am aware, this has not previously been discussed; other workers (Harris and Gunstad, 1936; Warburton, 1961) and I (James, 1961) have been too engrossed with the possibilities of curve-fitting to notice that it may easily interfere with frequencies of women to be expected with given combinations of live births and spontaneous abortions.

Suppose that a family size of two were universally desired, and suppose further that contraceptive technique were flawless. Then (ignoring the small number of matings characterized by involuntary secondary sterility) it would follow that every mating in which the completed family size involved two pregnancies would, in fact, comprise two live births. This is because those matings in which one or both of the first two pregnancies aborted, would engage in a further pregnancy, while those in which both pregnancies yielded live births would refrain from further reproductive efforts. In general, it would follow that every mating involving n pregnancies ($n = 2^+$), would involve n-2 abortions. Of course, neither of the conditions outlined is perfectly observed, but while they operate at all, it would be expected that those matings involving n pregnancies ($n = 3^+$), would be characterized by a reduction in variance.

It is, therefore, necessary to examine the extent to which these conditions *are* operating to see how much they may be expected to modify variance in this fashion.

1) It seems accepted that there is a general tendency for couples to think that a two-child family is the best size (Kiser and Whelpton, 1958), although it must be admitted that completed family size does not correlate highly with family size preference stated at the time of marriage (Westoff, Mishler and Kelly, 1957).

2) The efficiency of contraceptive technique was studied by Pearl (1932) who proposed the formula $R = \frac{\text{Total number of conceptions}}{\text{Total months of exposure}} \times 1200$ as a measure of conception rate. In a study by Westoff, Potter, Sagi and Mishler (1961) it was found that of a sample of 1,165 white couples in seven of the largest cities in the U. S., 917 (79 per cent) had used contraceptive methods (of various sorts) for an aggregate of 28,607 months. The number of accidental pregnancies was 534, giving a failure rate of R = 22.4 conceptions/100 years of exposure. In contrast, it has been estimated (Tietze, 1959) that in the absence of contraception, R is of the order of 80 conceptions/100 years of exposure. So it may be taken as established that in contemporary America, contraception is extremely prevalent and relatively efficient. The effect it has on the relation between abortion rates and completed gravidity size is exemplified forcibly in the admittedly unrepresentative sample of Reed and Kelly (1958). The women in this sample had volunteered to participate as subjects in a longitudinal study of marital compatibility and were selected simply for their willingness to cooperate in the study. (I call them unrepresentative only because their mean intelligence was above average and because their use of contraceptive techniques was attended with more than usual success.) Among Reed and

Kelly's 2-gravidae, the incidence of abortion is 5 per cent. Among the first two pregnancies of their 3-gravidae, the comparable figure is 17 per cent (ignoring induced abortions and counting stillbirths as spontaneous abortions).

If it be accepted that selective application of contraception is responsible for this, it would follow that standard curves fitted to such data could form only the basis for tenuous conclusions. For unless one could estimate the extent to which the frequencies had been disrupted, one could make no firm inference even if one were able to fit the distributions.

However, this line of argument would seem applicable only when the abortion rate in families of n-gravidae is markedly less than in the first n pregnancies of (n+1)-gravidae.

TABLE 3. PREGNANCIES OF WOMEN IN THE ISR SAMPLE. FOR GRAVIDAE-(n+1), THE ABORTION RATE WITHIN THE FIRST N PREGNANCIES. CONTRASTED IS THE ABORTION RATE AMONG ALL PREGNANCIES OF THE CORRESPONDING N-GRAVIDAE

	n			
	2	3	4	5
Abortion rate In the first n pregnancies of (n+1)-gravidae	16.2	29.4	28.0	37.5
Abortion rate among all pregnancies of n-gravidae	9.1	18.0	27.0	28.0

In all cases, percentages are for totals of more than 100 pregnancies.

Table 3 makes this comparison for families in the ISR sample for values of n from n=2 to n=5. The rate in the first two pregnancies of 3-gravidae is almost double the rate in 2-gravidae. For other n, it may be noted that although the rates are always higher in the first n pregnancies of (n+1)-gravidae than the rates in n-gravidae, the proportional difference in no other case is so great. So in these cases, the effect of additional fertility after abortion will be ignored for purposes of curve-fitting.

TESTING FOR SEGREGATION OF ABORTION PROBABILITY

It was proposed to test for segregation of abortion-probability by examining the fit to the double binomial $\nu_1 (p_1 + q_1)^n + \nu_2(p_2 + q_2)^n$ (James, 1961). For each gravidity group, q_1 and q_2 were estimated, and then estimates of q_1 and q_2 for the whole sample were derived by weighting the separate estimates according to the number of women in the groups from which the estimates were made. Lastly, these over-all estimates of q_1 and q_2 were used to estimate ν_1/ν_2 separately for each gravidity group. The rationale of this was that if the selectivity mentioned were very powerful, then, of course, the fit could not be expected to be good. However, if it were weak, then for each gravidity group the ratio ν_1/ν_2 (i.e., the ratio of abortion-prone to abortion-resistant women in the gravidity group) would be expected to vary from group to group, increasing with gravidity. Then, within each gravidity group, the frequencies of women with 0,1,2...n abortions should approximate to the sums of the appropriate terms of the double binomial. The data for 2-gravidae were discarded as showing too much evidence of the selectivity. For the sample of 3, 4, 5 and 6-gravidae, the weighted estimates of q_1 and q_2 were 0.530949 and 0.104352, respectively, for the abortion-prone and abortion-resistant women (where $q = 1-p$ is the probability of aborting a pregnancy).

The same gravidity group frequency distributions of abortions were also fitted to (1) negative binomials to test the hypothesis that abortion-probability is a unimodal positively skewed variable (Greenwood and Yule, 1920) and (2) Skellam's distribution (Skellam, 1948; Edwards, 1958) to test the hypothesis that abortion-probability is a β-variate. (With small variance, at any rate, the β- and normal distributions are similar, and it is reasonable to test whether a biological parameter like p, with a small range of variation, may be nearly normally distributed.) For brevity this hypothesis will be referred to as the Skellam hypothesis. Table 2 shows the results of these fits.

Chi-square values were computed for all fits. In all cases where the expected frequencies were less than five, the cell values were pooled until this value was exceeded. The results were as follows:

For the double binomials, chi-square $= 6.893$; $0.1<p<0.2$ with 4 d.f.
For the negative binomial, chi-square $= 4.463$; $0.1<p<0.2$ with 2 d.f.
For Skellam's distribution, chi-square $= 1.537$; $0.5<p<0.7$ with 2 d.f.

Discussion

Extended discussion at this point would be superfluous as there is little to choose between the distributions here.

It is difficult to assess the effect of selective application of contraception on the frequencies. The ideal sample for the present purpose would be one in which contraception was either inefficient or not extensively practiced. However, so far as I am aware, no appropriate recent data have been published on such a sample. *Faut de mieux,* one has recourse to data gathered at a time when contraceptive propaganda was impassioned, illegal (in the U.S. Mail) and relatively inefficient (Stopes, 1927), in contrast to the bland product of the 1930's (McCarthy, 1954). The trouble about such data is that (following the tradition of more delicate days), they fail to separate induced from spontaneous abortions.

I shall describe an attempt to fit one such set of data to double binomials, negative binomials and to Skellam's distribution.

Data collected prior to 1921 have been presented by Harris and Gunstad (1936). For a sample of foreign-born women resident in the U.S., they gave the frequencies with each possible combination of numbers of live births and spontaneous abortions. These women were ascertained by a visit to an obstetric hospital. Harris and Gunstad were aware of some of the consequences of their mode of ascertainment: If the outcome of the ascertainment-pregnancy is included, the incidence of abortion will be underestimated because abortions have a smaller chance of hospitalization than live births. Instead, Harris and Gunstad elected to ascertain by a live birth which they then ignored; none of their data has been contributed by women who aborted their every pregnancy, so it is clear that bias may remain. Nevertheless, the bias is probably not great.

TABLE 4. WOMEN IN THE HARRIS AND GUNSTAD SAMPLE WITH 2, 3, 4, 5, 6 AND 7 PREGNANCIES. FREQUENCIES OF WOMEN OBSERVED AND EXPECTED ON THE DOUBLE BINOMIAL, SKELLAM'S DISTRIBUTION AND THE NEGATIVE BINOMIAL

		Abortions 0	1	2	3	4	5	6	7	Total
2 Pregnancies	O	449	121	20						590
	D	441.9	119.5	28.6						590.0
3 Pregnancies	O	228	94	30	8					360
	D	243.5	78.5	30.9	7.2					360.0
	S	228.8	91.7	32.3	7.2					360.0
	N	225.3	100.2	27.3	5.9					358.7
4 Pregnancies	O	141	44	22	7	2				216
	D	134.1	47.9	22.3	9.9	1.8				216.0
	S	140.2	46.3	19.8	7.7	2.1				216.0
	N	136.9	53.0	17.8	5.7	1.8				215.2
5 Pregnancies	O	69	34	24	12	3	1			143
	D	82.4	32.0	15.2	9.4	3.5	0.5			143.0
	S	67.0	38.9	21.5	10.5	4.1	1.0			143.0
	N	63.8	44.3	21.3	8.7	3.2	1.1			142.4
6 Pregnancies	O	56	22	13	7	1	0	0		99
	D	53.3	22.6	10.1	7.6	4.1	1.2	0.2		99.0
	S	53.8	26.6	11.9	4.7	1.6	0.4	0.1		99.0
	N	52.7	28.6	11.5	4.1	1.4	0.4	0.1		98.9
7 Pregnancies	O	31	12	6	4	1	3	1	0	58
	D	29.3	13.6	5.6	4.5	3.2	1.4	0.4	0.0	58.0
	S	31.5	10.9	6.3	4.0	2.6	1.6	0.8	0.3	58.0
	N	29.1	13.9	7.1	3.7	2.0	1.0	0.6	0.3	57.6

O = observed.
D = double binomial.
S = Skellam's distribution.
N = negative binomial.

The fits to the three theoretical distributions are shown in table 4. In Harris and Gunstad's data, abortion rates did not vary much with gravidity at the time of ascertainment. Hence, there seemed no advantage in estimating ν_1/ν_2 separately for each gravidity group. So weighted averages of q_1 and q_2 were first computed, and then an over-all estimate of ν_1/ν_2 derived therefrom.

The results were:

For the double binomials chi-square = 21.131; $0.2>p>0.1$ with 15 d.f.
For the negative binomials chi-square = 11.58; $0.05>p>0.02$ with 5 d.f.
For Skellam's distribution chi-square = 3.054; $0.7>p>0.5$ with 5 d.f.

Again, the best fit is yielded by Skellam's distribution, but the present results can scarcely be said to clinch the matter.

A Further Test

The apparent superiority of the Skellam hypothesis suggests that an attempt to fit Whitehouse's (1930) data to Skellam's distribution might be attended with success. Table 5 shows the results of such an attempt.

Chi-square = 11.574, $p<0.01$ with 3 d.f.

I have already shown that these data can be reasonably fitted by double binomials (James, 1961) so the poor fit of Skellam's distribution might plausibly be regarded as crucial, if one were satisfied with the data. However, they confound induced and spontaneous abortions.

TABLE 5. WOMEN IN THE WHITEHOUSE SAMPLE WITH 4, 5 AND 6 PREGNANCIES. FREQUENCIES OF WOMEN OBSERVED AND EXPECTED ON SKELLAM'S DISTRIBUTION

		Abortions							
		0	1	2	3	4	5	6	Total
4 Pregnancies	O	81	39	6	7	3			136
	E	84.6	29.2	13.9	6.3	2.0			136.0
5 Pregnancies	O	42	31	16	3	1	2		95
	E	44.4	27.2	14.3	6.4	2.2	0.4		95.0
6 Pregnancies	O	27	15	5	6	2	2	0	57
	E	27.4	13.1	7.7	4.6	2.6	1.2	0.4	57.0

O = observed.
E = expected.

Conclusion

Skellam's distribution makes a good fit to the data of Harris and Gunstad and of the Institute for Sex Research but a poor fit to Whitehouse's data. The double binomial makes a fair (but unimpressive) fit to all three. It is possible that the anomalous nature of these results is attributable to characteristics of the data which render them questionably suitable for the present purpose; viz, the older data fail to discriminate between induced and spontaneous abortions, while more recent data show evidence of selective applications of contraception which violates the assumptions underlying the theoretical distributions.

ABORTION, MATERNAL AGE AND BIRTH ORDER

It has been commonly observed that spontaneous abortion rates correlate with birth order (Hudson, and Rucker, 1945; Javert, 1957; Rucker, 1952; Schoeneck, 1953; Stevenson, and Warnock, 1958; Shapiro, Jones, and Densen, 1962) and with maternal age (Gebhard and *et al.* 1958; Javert, 1957; Rucker, 1952; Stevenson and Warnock, 1958; Tietze, Guttmacher and Rubin, 1950). To the knowledge of this writer, however, only one attempt has been made to sort out the relative influence of these two variables (Warburton, 1961). However, in view of the empirical concurrence of Shapiro *et al.* (1962) with Erhardt and Jacobziner (1956) that the relationships are not linear, it would seem that Warburton's conclusions from a linear regression analysis may be misleading.

Be that as it may, it is usual to infer from the well-documented correlations that a woman's risk of aborting a pregnancy increases both with her age and with birth order (Javert, 1957). I shall call this the "causal" hypothesis. Its advocates might invoke, for instance, explanations involving:

(1) gradually deteriorating features of the intrauterine environment, or
(2) degradation of the ovum in the interval between the differentiation of the primary oocytes (possibly before puberty) and ovulation, or
(3) cumulative susceptibility of the maternal gonads to lethal mutagenic agents.

Of particular interest in this connection is the association of some forms of chromosomal anomalies with maternal age. Chromosomal anomalies have been shown to be associated with some spontaneous abortions (Penrose and Delhanty, 1961; Delhanty, Ellis and Rowley, 1961; Schmid, 1962) but the types of anomaly involved (triploidy and reciprocal translocations) have not, to my knowledge, been linked with maternal age.

It might be observed that nondisjunction of chromosome number 21 presumably gives rise to an equal number of monosomics as it gives to trisomic mongols, the monosomics dying, however, in utero. Such a mechanism might be expected to be intimately linked with maternal age; but since it would occur in about one pregnancy in 600 (the incidence of mongolism), it could be expected only to account for perhaps one abortion in 100.

During the remainder of this report this type of "causal" hypothesis will be questioned. Instead, data will be presented to support what will be called the 'artifact' hypothesis, viz that:

(1) Some women (here called "abortion-prone") are more likely to abort their pregnancies than other "abortion-resistant" women.
(2) Abortion-prone women have more pregnancies on the average than abortion-resistant women.
(3) Abortion-prone women have pregnancies at higher ages on the average, and
(4) The combination of these facts is mainly responsible for the observed correlations of abortion rate with maternal age and with gravidity.

It will be argued that the high spontaneous abortion rates for advanced age and gravidity categories are due to the higher proportions of abortion-prone women in these categories.

The Sample

The data used in the present analysis were elicited partially from the ISR Sample. Other data were provided by 822 additional women who were also interviewed by I.S.R. staff. These women also were white and had not been to prison, but they differed from the ISR Sample in that they: (a) were 30 plus years of age at the time of their marriage, or (b) were 36 minus years at the time of interview (or both).
I shall call these 822 women the ISR Sample 2.

In women in the ISR Sample the percentages of pregnancies aborting in the first five birth orders were 15.6, 13.7, 20.4, 20.0, and 29.6. For subsequent birth orders, the over-all percentage was 25.4. In the ISR Sample the ages at pregnancy were coded in 5-year intervals (20 and less = 1; 21-25 = 2, ...36 and over = 5). The percentages of pregnancies aborting during these five coded maternal ages were, respectively, 15.2, 20.2, 20.6, 22.0, and 27.5. Each of these percentages is based on a total of more than 70 pregnancies, so that the over-all rise in each case is clearly not attributable to chance.

Method: Analysis

The inference of a maternal age effect in spontaneous abortion has hitherto been drawn from the correlation of spontaneous abortion rates with birth order and with maternal age (correlations which are exemplified, as just noted, in the present data). However, these correlations could exist even if the causal hypothesis were false. This possibility may be tested by analyzing the data in a manner suggested by Slater (1962). His description of his method may be quoted:

> "When an individual comes mth in order of a sibship of n individuals —i.e., in the total of children borne by his mother—his ordinal position may conveniently be designated by the figure (m-1)/(n-1). This expression varies in value between the limits of 0 and 1, with a mean value which in a random collection of individuals tends towards 0.5. Within sibships of a stated size the values are not normally distributed, since each ordinal position is equally probable; but the means of values obtained on a series of individuals will tend to be normally distributed. The variance of values of this expression is easily calculated, so that the probability of a deviation from the expected mean of 0.5 can be reliably estimated. Not only the expected mean but also the expected variance of a series of observations may be calculated; for it is readily shown that the average theoretical contribution of each single observation to the total variance is (n+1)/12(n—1)—an expression which takes high values in small sibships and approximates to 1/12 as the sibship size increases."

In contrast to the Greenwood-Yule Method (Greenwood and Yule, 1914), Slater's analysis offers a means of detecting heterogeneity.

Findings: Birth Order

Tables 6 and 7 show the distribution of birth order of spontaneous abortions in each of the two samples; table 8 shows how the mean birth order, the

TABLE 6. ORDER OF BIRTH OF 241 SPONTANEOUS ABORTIONS IN THE ISR SAMPLE

Sibship Size	Order in Sibship 1	2	3	4	5	6	7	8	9	10
1	19									
2	11	13								
3	18	9	15							
4	22	16	18	12						
5	11	7	6	8	11					
6	4	5	5	4	4	3				
7	2		1	2	3	2	4			
8					1			1		
9										
10	1								1	1
11		1								

TABLE 7. ORDER OF BIRTH OF 180 SPONTANEOUS ABORTIONS IN THE ISR SAMPLE 2

Sibship	Order in Sibship 1	2	3	4	5	6	7	8	9
1	40								
2	20	23							
3	19	14	11						
4	6	6	7	8					
5	1	4	2	2	3				
6	1	1	1	1	1				
7	2	1	1	1	1	1	1		
8									
9	1								

variance and the standard error of the mean have been calculated for the pooled sample. The pooling is felt to be justified by the similarity of the two samples. Of course, by including a group of women with short reproductive lives (the ISR Sample 2) any age-effect would be lessened. But it may be verified that the relevant parameters of the two distributions are very similar. The principal conclusion is that the mean birth order of the abortions was 0.4846 with a standard error of 0.02157. These values are compatible with the hypothesis that birth order *per se* has no influence on the probability that a pregnancy will abort. It is true that the total variance observed, 60.81, is slightly higher than the expected value of 57.82, so the possibility of heterogeneity is not ruled out, although the limited extent of this difference would seem to rule out any marked age-effect in the majority of cases.

In interpreting these results, one makes the assumption (as one does with the Greenwood-Yule method) that fertility is not affected by an affected birth. If fertility were increased after such a birth, the analysis would yield the spurious suggestion that abortion risks are higher in the lower birth orders. It has been shown that this assumption is violated—a woman is more likely to engage in a further pregnancy after an affected birth. However, this excess fertility diminishes with birth order; to demonstrate this, data were taken on those ISR women who had aborted an arbitrarily chosen value of 30 per cent or more of their pregnancies. They will be called the "abortion-prone" subsample. Within this subsample the incidence of spontaneous abortion among *terminal* (*i.e.,* for each woman, the last pregnancy in her history) pregnancies was compared with the corresponding figure for their other pregnancies. For this purpose, women with only one pregnancy were omitted, and in those cases where the history ended with an induced abortion, the terminal pregnancy is taken as the last one which is not artificially terminated. The incidence of spontaneous abortion among the terminal pregnancies of abortion-prone women was 50.7 per cent and the incidence of spontaneous abortion among other pregnancies of abortion-prone women was 53.5 per cent. These incidences seem sufficiently close to warrant the conclusion that an abortion is followed only by additional fertility if it occurs relatively early in the sibship (otherwise these terminal pregnancies would show a less marked tendency to abort). This being so, the spurious negative birth-order effect would not be expected to be very great in the present case. It follows that if there really *is* a positive birth-order effect (*i.e.,* if the "causal" hypothesis is true), then it must have been very slight to have been swamped by a statistical artifact which it has been argued, must be small.

So it seems to follow that there is little evidence for the causal hypothesis; *per se* neither birth order nor, by inference, maternal age affect the probability that a pregnancy will abort.

Maternal Age

It is usual, in identifying a maternal age-effect, to contrast the frequency distribution of maternal ages of affected births with a comparable distribution for normal births. The maternal age distribution for spontaneous abortions and for all live births in the ISR Sample are contrasted in Fig. 1.

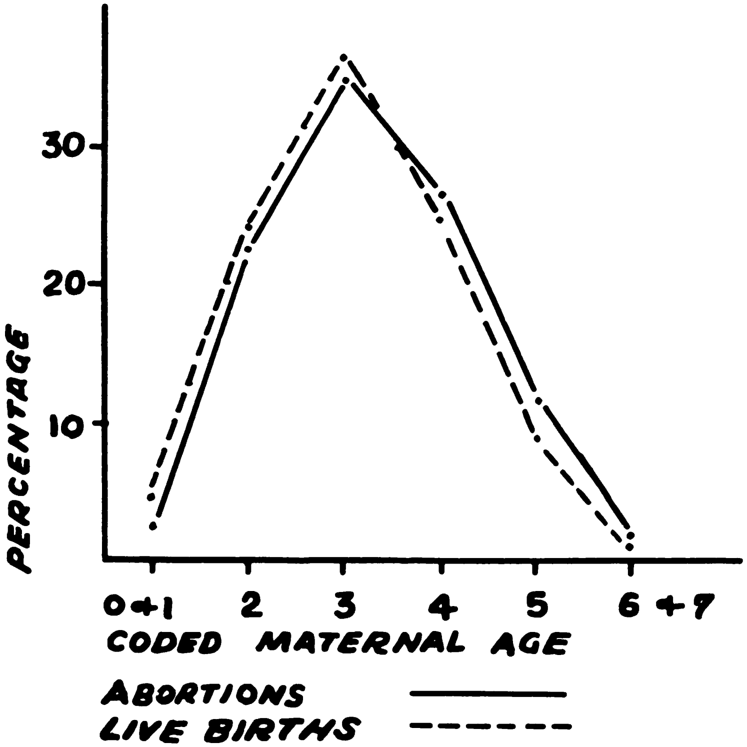

FIG. 1. Pregnancies in the ISR Sample. Percentages of total abortions and of total live births occurring at the given coded maternal ages.

This point will be treated cursorily only for two reasons: (a) It is debatable whether any available maternal age distribution is strictly comparable with the distribution for abortions here presented because it is known that the ISR Sample is not a representative sample of the American population (Gebhard *et al.,* 1958, pp. 18-23); (b) in any case, this form of analysis does not discriminate between the "causal" and the "artifact" hypotheses.

For these reasons the question of maternal age will not be further treated. This perhaps is not too serious, for as Slater (1962) says: "Even when we are primarily interested in maternal age, we may find that birth order supplies more reliable information...it may not be safe to compare maternal age for groups derived from different regions, different social classes, or different epochs. The subject's own sibship provides the control data which can be relied on to equalize such adventitious differences, if the datum taken is birth order."

A Further Test

To put the two hypotheses to a test, it was conjectured that if the causal hypothesis were true, then the correlations of abortion rates with maternal age and with gravidity should appear in at least one of the subsamples, the abortion-prone and the abortion-resistant subsamples. To check this, spontaneous abortion rates were computed by 5-year age intervals within both of the ISR subsamples. Secondly, spontaneous abortion rates were computed by gravidity rank within each of the subsamples (for this purpose, induced abortions were acknowledged in the following sense: for a woman whose history comprised an induced abortion for her first pregnancy and a spontaneous abortion for her second, only one entry is recorded—a spontaneous abortion for gravidity rank 2).

In the subsamples, the results for the lowest two maternal age categories were pooled. Then the percentages of pregnancies aborting in advancing age categories in the abortion-prone subsample were 58.4, 52.7, 56.2 and 53.6. The corresponding figures for the abortion-resistant subsample were 2.2, 3.5, 2.6 and 2.9. The percentages of pregnancies aborting in the first four birth orders in the abortion-prone subsample were 60.8, 55.0, 57.3 and *46.4*. For subsequent birth orders, the over all percentage was *53.0*. The corresponding figures for the abortion-resistant subsample were 2.3, 0.3, 2.9, *4.3* and *5.3*. The percentages italicized are for totals of between 50 and 100; all other totals exceed 100. One would conclude that spontaneous abortion rates remain largely unaffected by age. The figures for birth order are not so conclusive. In abortion-prone women there seems no evidence for a birth order effect, but in abortion-resistant women there is a slight rise in incidence from the second birth rank onwards. However, even if this rise is not due to chance, it is associated only with a small minority of abortions.

It is concluded that the lack of association of spontaneous abortion rates with age or with gravidity within either of these subsamples strongly militates against the theory that there is a direct causal connection between age and/or gravidity and the great majority of spontaneous abortions.

Assuming then, that the "causal" hypothesis is not true, it is interesting to examine the basis of the correlations which, confusingly, lend it credence. For this purpose, the mean number of pregnancies in the abortion-prone and abortion-resistant subsamples will be contrasted. It should be noted at the outset that the following considerations merely attempt to explain the origin of the correlations which make the "causal" hypothesis plausible; they are in no way

TABLE 8. CALCULATION OF MEAN BIRTH ORDER OF 362 SPONTANEOUS ABORTIONS FROM SIBSHIPS OF 2 OR MORE IN THE POOLED SAMPLE AND OF STANDARD ERROR OF MEAN

Sibship Size	No.	Sum of Values	Sum of Squares
2	67	36.0000	36.0000
3	86	37.5000	31.7500
4	95	44.0000	33.5556
5	55	28.2500	22.3125
6	30	13.6000	9.2000
7	22	12.5000	9.8611
8	2	1.5714	1.3265
9	1	0.0000	0.0000
10	3	1.8889	1.7901
11	1	0.1000	0.0100
Totals	362	175.4103	145.8058
Mean		0.4846	
Correction term			84.9966
Total variance			60.8092
S. E. of mean		0.02157	

intended to add directly to the evidence against the "causal" hypothesis. For if the "causal" hypothesis were true, then women ascertained by aborting would, on the average, be older at pregnancy and have had more pregnancies anyway. For this observation I am indebted to Professor L. S. Penrose.

Mean Number of Pregnancies of Abortion-Prone and Abortion-Resistant Women

In the search for an explanation of the apparently unabated incidence of several disorders against which there is known to be genetic selection, it has been noted that parents are inclined to compensate for a fetal or infantile death by initiating a further pregnancy. This has been reported, for instance, in microcythemia (Silvestroni, Bianco, Montalenti and Siniscalco, 1950), acholuric jaundice (Race, 1942), and erythroblastosis fetalis (Glass, 1950). Such a tendency to compensate for fetal loss has also been reported among women with a high incidence of spontaneous abortion (Winkelstein, Stenchever and Lilienfeld, 1958). However, since these abortion-prone women had been ascertained by having survived one or more myocardial infarctions, the point needs clarification.

Using a t test, it was found that the abortion-prone subsample had had a higher mean number of pregnancies (2.79) than the abortion-resistant subsample (2.42). ($t = 3.07$, $p < 0.01$.)

The causes of these additional pregnancies among the abortion-prone women are not germane to this report; however, since it seems that they may be readily identified, I shall try to identify them. I have no data on the contraceptive practice of the ISR Sample; however, data provided by Reed and Kelly (1957) on a comparable group of women were examined. For each woman, the third pregnancy was classified by whether it was live or aborted, and the subsequent pregnancy (*i.e.*, the fourth) was classified by whether it was preceded by contraceptive efforts or not. Pregnancies between which an intervening induced abortion had occurred were not counted, and stillbirths were counted as spontaneous abortions. Table 9 shows the frequencies (in Reed and Kelly's sample) of contraceptive practice prior to the fourth pregnancy, by the outcome of the

TABLE 9. PREGNANCIES OF WOMEN IN REED AND KELLY'S (1957) SAMPLE

	Frequencies of Planned vs. Unplanned Pregnancies of Gravidity Rank 4 by the Outcome of the Immediately Preceding Pregnancy	
Outcome of preceding (index) pregnancy	Subsequent Pregnancy (Unplanned despite contraception)	(No planned contraception)
Abortion or stillbirth	1	18
Live birth	10	23

For this partition and the more extreme one, the sum of Fisher's exact probabilities is $p = 0.032$.

index (third) pregnancy. The sum of Fisher's exact probabilities for this partition and the more extreme one is $p = 0.032$. It may be verified that similar extreme partitions are yielded if the first or second pregnancies are chosen as index. It may be inferred then that spontaneous abortions are more likely than live births to be followed by planned pregnancies (*i.e.*, pregnancies occurring in the absence of contraceptive efforts).

Fisher (1930) had suggested that families tend to fill up to a certain average size for a given population or stratum within the population, and the point has received confirmation from, *inter alia,* the Indianapolis Study (Kiser and Whelpton, 1958). It seems that for many people the ideal family size is two children; it is suggested therefore that abortion-prone women repeatedly undertake pregnancies in order to achieve this ideal; it simply takes more pregnancies in their case.

Mean Age At Pregnancy of Abortion-Prone and Abortion-Resistant Women

It has been argued that the correlation of spontaneous abortion rates with gravidity is due to the fact that abortion-prone women have more pregnancies on the average. It may also be shown that abortion-prone women have pregnancies at more advanced ages on the average. In the ISR Sample, the ages at pregnancy were coded in 5-year intervals (16-20 = 1; 21-25 = 2....41-45 = 6). The mean coded age at pregnancy of abortion-prone women was 3.29, while the corresponding figure for abortion-resistant women was 3.09. For the difference, $t = 4.02$ and $p<0.01$. It follows that within maternal age categories, the proportion of gravidae who are abortion-prone correlates with maternal age.

SUMMARY AND CONCLUSIONS

1. Abortion-probability varies from woman to woman but remains relatively constant within a given woman.
2. Abortion-prone women have more pregnancies, on the average, than other women.
3. Abortion-prone women have their pregnancies at higher ages, on the average, than other women.
4. These facts (rather than a direct causal nexus) account, partially at least, for the correlation of spontaneous abortion rates with maternal age and with gravidity.
5. The outcomes of adjacent pregnancies show no evidence of positive correlation with one another.
6. Selective application of contraceptive techniques after families have reached the desired number of live births, interferes with the randomness assumed by interpretations based on curve-fitting procedures.
7. The data here examined seem inadequate to discriminate between the hypotheses that abortion-probabilities are: a) normally distributed, and b) bimodally distributed.
8. This question is unlikely to be settled (using the present methods anyway) until data are available which separate induced from spontaneous abortions in a population which does not use contraceptive methods.

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REFERENCES

DELHANTY, J. D. A., ELLIS, J. R., AND ROWLEY, P. T 1961. Triploid cells in a human embryo. *Lancet* 1: 1286.

EDWARDS, A. W. F. 1958. An analysis of Geissler's data on the human sex-ratio. *Ann. Hum. Genet.* 23: 6.

EDWARDS, A. W. F. 1960. The meaning of binomial distribution. *Nature* (Lond.) 186: 1074.

ERHARDT, C. L., AND JACOBZINER, H. 1956. Ectopic pregnancies and spontaneous abortions in New York City—incidence and characteristics. Amer. J. Public Health. 46: 828.

FISHER, R. A. 1930. *The Genetical Theory of Natural Selection.* Oxford: Clarendon Press.

FISHER, R. A. 1932. *Statistical Methods for Research Workers.* 4th ed. Edinburgh. Oliver & Boyd.

GEBHARD, P. H., POMEROY, W. B., MARTIN, C. E., AND CHRISTENSON, C. 1958. *Pregnancy, Birth and Abortion.* New York: Harper and Bros.

GLASS, B. 1949. The relation of Rh incompatibility to abortion. *Amer. J. Obstet. Gynec.* 57: 323.

GLASS, B. 1950. The action of selection on the principal Rh alleles. *Amer. J. Hum. Genet.* 2:269.

GREENWOOD, M., AND YULE, G. U., 1914. On the determination of size of family and of the distribution of characters in order of birth from samples taken through members of the sibships. *J. Roy. Statist. Soc.* 77: 179.

GREENWOOD, M., AND YULE, G. U. 1920. An inquiry into the nature of frequency distributions representative of multiple happenings with particular reference to the occurrence of multiple attacks of disease or of repeated accidents. *J. Roy. Statist. Soc.* 83: 255.

HARRIS, J. A., AND GUNSTAD, B. 1936. The measurement of the individuality of women with respect to their capacity for bringing the fetus to term. In: *J. Arthur Harris, Botanist and Biometrician.* Ed. Rosendahl, C. O., Ross, A. G., and Burr, G. O. Minneapolis: Univ. of Minn. Press.

HUDSON, G. S., AND RUCKER, M. P. 1945. Spontaneous abortion. *J. A. M. A.* 129: 542.

JAMES, W. H. 1961. On the possibility of segregation in the propensity to spontaneous abortion in the human female. *Ann. Hum. Genet.* 25: 207.

JAMES, W. H. 1962. On the probability that an untreated habitual aborter will abort a current pregnancy. *J. Obst. Gynaec. Brit. Commonw.* 69: 606.

JAMES, W. H. 1963. The problem of spontaneous abortion X: the efficacy of psychotherapy. *Amer. J. Obstet. Gynec.* 85: 38.

JAVERT, C. T. 1957. *Spontaneous and Habitual Abortion.* New York: McGraw-Hill.

KINSEY, A. C., POMEROY, W. B., AND MARTIN, C. E. 1948. *Sexual Behaviour in the Human Male.* Philadelphia: Saunders.

KISER, C. V., AND WHELPTON, P. K. 1958. Social and psychological factors affecting fertility XXXIII: Summary of chief findings and implications for future studies. Milbank Mem. Fund Quart. 36: 282.

McCarthy, M. 1954. Dottie makes an honest woman of herself. *Partisan Rev.* 21: 34.

Pearl, R. 1932. Contraception and fertility in 2000 women. *Hum. Biol.* 4: 363.

Penrose, L. S., and Delhanty, J. D. A. 1961. Triploid cell cultures from a macerated foetus. *Lancet* 1: 1261.

Race, R. R. 1942. On the inheritance and linkage relations of acholuric jaundice. *Ann. Hum. Genet.* 22: 165.

Reed, T. E., and Kelly, E. L. 1958. The completed reproductive performances of 161 couples selected before marriage and classified by ABO blood group. *Ann. Hum. Genet.* 22: 165.

Rucker, M. P. 1952. Spontaneous abortions: too many or too few? *J. Int. Coll. Surg.* 17: 328.

Schmid, W. 1962. A familial chromosome aberration associated with repeated abortions. Paper read to the American Society for Human Genetics.

Schoeneck, F. J. 1953. Pregnancy patterns and fetal salvage. *Obstet. Gynec.* (N. Y.) 1: 610.

Shapiro, S., Jones, E. W., and Densen, P. M. 1962. A life table of pregnancy terminations and correlates of fetal loss. *Milbank Mem. Fund Quart.* 40:7.

Silvestroni, E., Bianco, I., Montalenti, G., and Siniscalco, M. 1950. Frequency of microcythaemia in some Italian districts. *Nature* (Lond.) 165: 682.

Skellam, J. G. 1948. A probability distribution derived from the binomial distribution by regarding the probability of success as variable between the sets of trials. *J. Roy. Statist. Soc.* 'B' 10: 257.

Slater, E. T. O. 1962. Birth order and maternal age of homosexuals. *Lancet* 1: 69.

Stevenson, A. C., and Warnock, H. A. 1958. Observations on the results of pregnancies in women resident in Belfast. *Ann. Hum. Genet.* 23: 382.

Stopes, M. C., 1927. *Contraception, its theory, history and practice.* 2nd ed. London: Bale, Sons & Danielsson.

Swed, F. S., and Eisenhart, C. 1943. Tables for testing randomness of grouping in a sequence of alternatives. *Ann Math. Statist.* 14: 83.

Tietze, C. 1959. The clinical effectiveness of contraceptive methods. *Amer. J. Obstet. Gynec.* 78: 650.

Tietze, C., Guttmacher, A. F., and Rubin, S. 1950. Unintentional abortion in 1497 planned pregnancies. *J. A. M. A.* 142: 1348.

Warburton, D. 1961. *Factors in the aetiology of spontaneous abortion.* Unpublished Ph. D. thesis, McGill University, Montreal.

Warburton, D., and Fraser, F. C. 1959. Genetic aspects of abortion. *Clin. Obstet. Gynec.* 2: 22.

Westoff, C. F., Mishler, E. G., and Kelly, E. L. 1957. Preferences in size of family and eventual fertility twenty years after. *Amer. J. Sociol.* 62: 491.

Westoff, C. F., Potter, R. G., Sagi, P. C., and Mishler, E. G. 1961. *Family Growth in Metropolitan America.* Princeton: Princeton University Press.

Whitehouse, B. 1930. Discussion on the causes of early abortion and sterility. *Proc. Roy. Soc. Med.* 23: 248.

Winkelstein, W., Stenchever, M. A., and Lilienfeld, A. M. 1958. Occurrence of pregnancy, abortion and artificial menopause among women with coronary artery disease. *J. Chronic Dis.* 7: 273.