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FURTHER RESULTS FROM A HUMAN FERTILITY MODEL WITH A VARIETY OF PREGNANCY OUTCOMES *

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INTRODUCTION

THE factors involved in the process of human reproduction are so large in number and presumably so variable that any attempt at model-building requires considerable simplification of the underlying biological relationships. Relatively simple models have in the past, however, provided useful insights into the quantitative approach to reproductive data, and it therefore seems worthwhile to persist in their study. Often, in fact, slightly restricted versions of more general models (Henry, 1953, 1961; Perrin and Sheps, 1964, 1965; Sheps, 1964b) permit explicit useful results that are not available for the general case. Hence they contribute more readily to an understanding of the nature of changes in the process produced by alteration of essential parameters. They may provide insight into problems such as: Can we predict how the birth rate would be affected if 45% of a population were to adopt a contraceptive of 80% effectiveness? Or we might ask, what would be the effect on the birth rate if fetal losses (miscarriages and stillbirths) were to be reduced by 75% or if induced abortions were legalized? If a woman uses a contraceptive that reduces the monthly probability of conception to 0.01, what are her chances of having at least two children in the course of ten years? What are useful and valid methods of evaluating the effectiveness of a contraceptive in clinical situations? (Potter, 1960a, 1960b, 1961; Perrin, 1966; Sheps, 1964a, 1966b; Sheps and Perrin, 1963, 1964; Tietze, 1962).

The chief utility of a stochastic model such as that presented here,

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of course, lies in the insight that it affords into the behavior of the biological process that the model describes. Even if one restricts his attention to populations assumed homogeneous with respect to the various fertility parameters, for example, a great deal can be learned concerning the source and amount of variation which occurs quite naturally in a biological system of this nature. The presence and effect of natural variation is often not well enough understood in complicated biological systems.

The model considered here includes provision for fetal wastage and a non-susceptible period following pregnancy, the duration of which depends on the pregnancy outcome. At the same time, it permits certain results, such as a closed expression for the probability of r births in y years, which cannot be obtained with the more general models of which it is a special case. The results developed below for this case include the distributions of intervals between births or the waiting time until the r -th birth.

After summarizing previous work, we shall present the model and our results, and conclude by illustrating applications such as have just been described. Other applications are illustrated in the references.

PREVIOUS WORK

As is described in more detail elsewhere (Sheps, 1966a), several authors have approached the problem of determining the distribution of the number of births by assuming that a susceptible nonpregnant woman has a fixed probability of becoming pregnant during a menstrual cycle (usually put equal to one month) and by making an allowance for the fact that when pregnancy ensues, another pregnancy is impossible while the first pregnancy lasts and for some time after its termination (Henry, 1953, 1961; Pearl, 1939; Potter, 1963; Tietze, 1962). Dandekar (1955) derived an expression for the probability of at most x live births in y years, considering only pregnancies that terminate in live births and treating the period of nonsusceptibility to pregnancy as fixed. Potter has added some provision for pregnancy wastage (Potter, 1961). Singh has proposed modifications of Dandekar's model, and has attempted to fit Dandekar's data to one such modification (Singh, 1963), still allowing, however, for only a single type of pregnancy outcome.

The problem of determining birth distributions has similarities to other biological problems (Weiss and Zelen, 1962) and particularly to the "counter" problem (Feller, 1957; Parzen, 1962). In the latter situation, a device ("counter") that registers the random arrival of

radioactive particles becomes temporarily incapable of registering new impulses for a random time after registering a particle. This inactive interval is known as "dead time" for the counter. In the model to be described, the human female is considered analogous to a counter mechanism with two kinds of impulses that produce a "dead time," or a state of nonreceptivity to further impulses. One type is a conception leading to a live birth and the other, a conception leading to a fetal loss. Each type of conception (registered particle) is followed by a nonsusceptible period, whose length depends on the type of conception. We are interested primarily in the recurrence pattern of live births, (*i. e.*, of one type of impulse), in the probability distribution of the number of live births that occur over a period, in the distribution of the intervals between successive live births, and in similar results.

The present authors have described a general model for this process which utilizes the theory of Markov Renewal Processes (Perrin and Sheps, 1964; Pyke, 1961), but which because of its complexity does not yield some of the simpler results obtained for the special case considered in this paper. This general model allows for more than one type of pregnancy, *e. g.*, with a given probability any pregnancy can terminate in either fetal death, stillbirth or a live birth. It also allows for variable periods of gestation and of nonsusceptibility to conception (infecundability) associated with each pregnancy. The duration of these periods are assumed to depend on the form of the pregnancy termination. Extensions to a heterogeneous population of couples with unequal monthly chances of conceiving or fecundability have been made (Sheps, 1964b). We have also reported (Sheps and Perrin, 1963) some results based on the special more restricted case (fixed "dead" or infecundable time) described in the following sections.

ASSUMPTIONS IN THE PRESENT CASE

(1) The discussion here will be primarily concerned with a homogeneous group of women (equal parameters) all of whom are susceptible to pregnancy at marriage. The unit of time, the duration of a menstrual cycle, is assumed equal to one month.

(2) During any cycle when a woman is susceptible to conception, the probability of conceiving (fecundability) is equal to ρ and is assumed to be constant during the period of observation.

(3) There is a fixed probability (α) that any pregnancy will end in a fetal loss (miscarriage, abortion, or stillbirth).

(4) A pregnancy which terminates in a live birth (L conception) is associated with an inability to conceive again at the times when the next $m - 1$ ovulations would otherwise occur following the conception (*i. e.*, duration of infecundable or nonsusceptible period is equal to m months), and a pregnancy that terminates in a fetal loss is associated with a similar infecundable period of w months. Each infecundable period consists of the period of pregnancy plus a postpartum infecundable period. The presentation and results that follow would be essentially unchanged if these component intervals were considered separately. For example, if m_1 and m_2 were the duration of pregnancy and the postpartum period, respectively, then $m_1 + m_2$ would be substituted for the m in the results.

(5) The treatment that follows considers the distribution of the number of months or trials between two events, including in the counting process the month in which the event occurs. For example, the probability that the first conception occurs in month t of marriage, ($t = 1, 2, \dots$) is $\rho(1 - \rho)^{t-1}$. If it is desired to focus on the waiting time, *i. e.*, to put $t = 0$ for the first month, obvious modifications are necessary (Sheps, 1964b).

As long as attention is focused on one type of conception, this model meets the definition of a general renewal process (Murthy, 1961; Smith, 1958). When it is taken more broadly, attention being given to all states that the woman may occupy (including susceptibility to pregnancy, the infecundable period associated with fetal loss, or the infecundable period associated with live births), with a variable length of stay in each type of infecundable period, it conforms to the definition of a zero-order Markov Renewal Process (Pyke, 1962). Further, it is easily shown that when the infecundable periods are treated as fixed, as in this paper, the process can be reduced to a finite Markov chain (Feller, 1957; Kemeny and Snell, 1960).

RESULTS UNDER THIS MODEL

Derivation. In accordance with our assumptions, let ρ represent the (constant) monthly probability of conception by a fecundable married female and let α be the probability that a given conception by that female will end in a fetal loss. It then follows that p , the monthly probability of an L conception, π , the monthly probability of a conception ending in a fetal loss, and q , the monthly probability of no conception, are given by the relations:

$$\begin{aligned}p &= (1 - \alpha)\rho, \\q &= 1 - \rho, \\\pi &= \alpha\rho,\end{aligned}$$

where $p + \pi + q = 1$.

It follows also that the probability that the r -th L (live birth) conception will occur in month t ($t = 1, 2, \dots$) in a marriage under this model is

$$p^r \sum_{v=0}^z \frac{(v + r + y - 1)!}{(r - 1)!v!y!} \pi^v q^y, \text{ for } r \geq 1, \quad (1)$$

where $y = t - (r - 1)m - vw - 1$ and z is the largest integer for which $zw \leq t - (r - 1)m - 1$.

With the further assumption that the r -th birth takes place nine months after the r -th L conception, Equation (1) then gives the probability of the r -th birth occurring in month $t + 9$.¹

The derivation of Equation (1) is straightforward. We know that the r -th L conception occurs in month t and that there have been $r - 1$ L conceptions previously, consuming a total of $(r - 1)m$ months. In the remaining $t - (r - 1)m - 1$ months there have been v conceptions that end in a fetal loss, with $0 \leq v \leq z$ and $zw \leq t - (r - 1)m - 1$, these conceptions tying up a total of vw months. This implies there were $y = t - (r - 1)m - vw - 1$ months in which a conception could have occurred but did not. The probability of such an outcome for any r, v

and y is $\frac{(r - 1 + v + y)!}{(r - 1)!v!y!} p^r \pi^v q^y$. Equation (1) is then obtained by

summing these probabilities over all possible values of v .

Let $N(t)$ be the number of L conceptions that occur in the interval $(1, t)$ for an individual marriage. The cumulative probability, $K_r(t)$, that the r -th L conception occurs in month t or sooner is equal to the probability that at least r such conceptions occur in the first t months of marriage, i. e., $\text{Prob}[N(t) \geq r]$. This is given by

$$K_r(t) = p^r \sum_{v=0}^z \sum_{y=0}^{t - (r - 1)m - vw - 1} \frac{(v + r + y - 1)!}{(r - 1)!v!y!} \pi^v q^y \quad (2)$$

where $zw \geq t - (r - 1)m - 1$. Equation (2) follows in the same manner as Equation (1) by simply noting that the number of months,

¹ In results concerning the expected number of live births in the $t + 9$ months it is only necessary to assume that the mean duration of pregnancy is 9 months.

y, during which pregnancy can occur but does not, can also vary in this case from 0 to $t - (r-1)m - vw - 1$ for each value of v .

The distribution of the number of L conceptions occurring in t months (and consequently the number of live births in $t + 9$ months) is given exactly by:

$$\text{Prob}[N(t) = r] = K_r(t) - K_{r+1}(t), \text{ where } K_0(t) = 1. \quad (3)$$

An alternative proof of (1) and (2) which yields other interesting results as well can be given by utilizing the generating functions of the waiting times of the process. As in the study of renewal processes generally (Cox, 1962), we can define S_r to be the month when the r -th L conception takes place. Then $\text{Prob}[N(t) \geq r] = \text{Prob}[S_r \leq t]$. If we represent by $P(t)$ the probability that the first L conception occurs at month t , the generating function of this probability is defined to be (Feller, 1957):

$$A(s) = \sum_{t=0}^{\infty} P(t)s^t.$$

It is not difficult then to show that

$$A(s) = \frac{ps}{1 - qs - \pi s^w}. \quad (4)$$

Analogously, the generating function for the interval between two L conceptions (or two live births), counting the month when the second L conception occurs, can be shown to be:

$$B(s) = \frac{ps^m}{1 - qs - \pi s^w}. \quad (5)$$

The moments of the respective birth intervals (under the assumption of a reproductive period of unlimited length) can be derived from (4) and (5). More important, the generating function S_r is the convolution:

$$P_r(s) = A(s)[B(s)]^{r-1} = \frac{p^r s^{(r-1)m+1}}{(1 - qs - \pi s^w)^r}. \quad (6)$$

The coefficient of s^t in the expansion of (6), *i. e.* the probability that the r -th L conception occurs in month t , is easily shown to be the expression given by Equation (1).

Further, if we designate this coefficient as $P(r, t)$, we have that the cumulative distribution function of S_r , or $\text{Prob}[S_r \leq t]$, is $\sum_{i=0}^t P(r, i)$ with a generating function:

$$K_r(s) = \sum_{t=0}^{\infty} \sum_{i=0}^t P(r, i) s^t = \frac{P_r(s)}{1-s}. \quad (7)$$

The coefficient of s^t in the expansion of (7) is then the expression given in (2).

Formulas for Calculating Probabilities. Calculations with Equation (2) are difficult. The following derivation yields an expression from which calculations can be made more easily with the aid of partial sums of binomial expansions.

Consider the situation in which v conceptions ending in a fetal loss occur before the r -th L conception. Since these conceptions will tie up a total of $v(w-1) + (r-1)(m-1)$ months excluding the months when conception takes place, the probability that the r -th L conception occurs in month t or sooner where $n' = t - (r-1)(m-1) - v(w-1)$, (i. e., $K_r(t)$ for a fixed v) is given by:

$$\sum_{x=v+r}^{n'} \left(\frac{n'}{x}\right) \rho^x (1-\rho)^{n'-x}, \quad (8)$$

that is, the probability of at least $r+v$ conceptions occurring in the available n' months.

Now the probability of v fetal loss pregnancies preceding the r -th L pregnancy is

$$\binom{r+v-1}{v} (1-\alpha)^r \alpha^v. \quad (9)$$

Hence, by multiplying (8) and (9) and summing over v , we have that:

$$Pr[N(t) \geq r] = K_r(t) = (1-\alpha)^r \sum_{v=0}^z \binom{r+v-1}{v} \alpha^v \sum_{x=r+v}^{n'} \left(\frac{n'}{x}\right) \rho^x (1-\rho)^{n'-x} \quad (10)$$

where $n' = t - (r-1)(m-1) - v(w-1)$ and $zw \geq t - (r-1)m - 1$.

Equation (10) holds for any value of α , the probability of a fetal loss. When α is taken to be equal to zero, Expression (10) reduces to:

$$Pr[N(t) \geq r] = \sum_{x=r}^n \left(\frac{n}{x}\right) \rho^x (1-\rho)^{n-x} \quad (11)$$

where $n = t - (r-1)(m-1)$, a relationship which may also be proven directly. The expression for the probability of at least r births in time $t+9$ thus reduces to one tail of a binomial distribution in this special

case, and it is possible to evaluate this probability without extensive calculations.

From (3) and (10) the probability that $N(t)$ takes on a specific value is easily obtained. Expressions (10)-(11) are simpler than those previously given for these probabilities. They may be evaluated with the help of published tables of the cumulative binomial distribution (Harvard University, 1955) or of the cumulative Poisson distribution. A program for evaluation of (1) on an electronic computer can also be written.

The Mean and Variance of $N(t)$. Exact values for the mean and variance of $N(t)$, under this model, may be calculated with the use of

expression (1). The mean itself is of course equal to $\sum_{r=1}^{\infty} K_r(t)$.

Asymptotic expression for $E[N(t)]$ and $\text{Var}[N(t)]$ as well as for higher moments of $N(t)$ as functions of the moments of the recurrence times are given by Murthy (1961) for the general renewal process, of which this model is a special case (Feller, 1957; Smith, 1958). As has been shown elsewhere (Perrin and Sheps, 1964) these formulas for the first two moments of $N(t)$ give a good approximation, under this model, to the true value of the mean and variance of the number of births when $t \geq 60$.

Further, it has been shown (Feller, 1957) that, given that the 2nd moment of the recurrence time is finite, as $t \rightarrow \infty$, $N(t)$ is asymptotically normally distributed, *i. e.*,

$$\text{Prob}[N(t) \geq \frac{t}{\mu} - \frac{\lambda\sigma}{\mu} \sqrt{\frac{t}{\mu}}] \rightarrow \Phi(\lambda) \quad (12)$$

where μ and σ^2 are, respectively, the **mean and variance** of the intervals between birth and $\Phi(\lambda)$ is the normal integral. In the special cases where we have been able to calculate these probabilities directly however, Eq. (12) does not yield satisfactory approximation to the exact values over a suitable range of t .

Provision for Additional Assumptions. To the results presented above, a provision for complete sterility may easily be added. Thus if the proportion of women who are at risk of pregnancy be put equal to f , then

$$\text{Pr}[N(t) = 0] = 1 - f + f(1 - \rho)^t$$

and

$$\Pr[N(t) \geq r] = fK_r(t) \text{ for } r > 0. \quad (13)$$

Furthermore, it is possible to provide for a heterogeneous population having a distribution of unequal values (ρ_i) of infecundability. In this case, the $\Pr[N(t) \geq r]$ becomes a weighted mean of the probabilities in (10), assuming that the probability of fetal loss (α) and the durations of the infecundable periods (m and w) are constant in this population.

MOMENTS AND CUMULANTS OF THE BIRTH INTERVALS

Generating functions for the cumulants of the relevant waiting times under the assumption of a reproductive period of unlimited length are given by the natural logarithms of expressions (4)-(6) with e^s substituted for s . Results for the first passage times and the recurrence times in a more general model have been given elsewhere (Perrin and Sheps, 1963). For the present special case, simpler expressions will suffice.

If we evaluate the consecutive derivatives of the cumulant generating function at $s = 0$ and let $F^{(j)} = \frac{q + w^j \pi}{p}$ the first four cumulants of the time until the first L conception are easily seen to be:

$$\begin{aligned} K_1 &= 1 + F^{(1)} \\ K_2 &= F^{(2)} + (F^{(1)})^2 \\ K_3 &= F^{(3)} + 3F^{(2)}F^{(1)} + 2(F^{(1)})^3 \\ K_4 &= F^{(4)} + 4F^{(3)}F^{(1)} + 3(F^{(2)})^2 + 12F^{(2)}(F^{(1)})^2 + 6(F^{(1)})^4. \end{aligned} \quad (14)$$

The cumulants of the interval between two L-conceptions are, of course, the same, with the exception of the first, which is $m + F^{(1)}$, for this case. Similarly, the n -th cumulant of the r -th L-conception can be shown from the generating function to be rK_n , with the exception of the first cumulant which is $(r-1)m + rF^{(1)} + 1$.

The respective moments can be obtained directly from the cumulants by well known relationships (Kendall and Stuart, 1958). For example, if μ_i is the i -th moment about the origin and K_i is the i -th cumulant:

$$\begin{aligned} \mu_1 &= K_1 \\ \mu_2 &= K_2 + K_1^2 \\ \mu_3 &= K_3 + 3K_2K_1 + K_1^3 \\ \mu_4 &= K_4 + 4K_3K_1 + 3K_2^2 + 6K_2K_1 + K_1^4. \end{aligned} \quad (15)$$

In particular, the first two cumulants are equivalent to the mean and variance respectively. Hence, for example, the mean month for the

occurrence of the r -th live birth is (assuming a 9 month gestation, on the average) :

$$\begin{aligned} E(S_r) + 9 &= (r-1)m + rF^{(1)} + 1 + 9 \\ &= (r-1)m + r\left(\frac{q + w\pi}{p}\right) + 10. \end{aligned} \quad (16)$$

Since the present model treats the duration of both gestation and post partum infecundability as fixed, the variance of the time until r -th L conception and the time until the r -th birth are identical and equal to

$$\text{Var}(S_r) = rK_2 = r\left\{\frac{q + w^2\pi}{p} + \frac{(q + w\pi)^2}{p^2}\right\}. \quad (17)$$

Provision for heterogeneity of fecundability (a distribution of ρ_i) complicates the expressions for the moments of the recurrence times considerably. Results for this situation are derived elsewhere (Sheps, 1964b).

THE PROCESS VIEWED AS A MARKOV CHAIN

In a previous publication (Perrin and Sheps, 1964), it was shown that the present model, without the restrictive assumption of constant durations of infecundability is an example of a Markov Renewal Process. With the assumptions in the present case, analogous results may be obtained by formulating the process as an ordinary Markov chain (Feller, 1957; Kemeny and Snell, 1960) with the states:

- S_0 : the nonpregnant, fecundable state,
- L_1 : a state corresponding to the month of conception leading to a live birth,
- L_2, L_3, \dots, L_m : states corresponding to the first, second, \dots , $(m-1)^{\text{th}}$ month of infecundability following the month during which the conception leading to a live birth occurs, and
- A_1, A_2, \dots, A_{w-1} : the corresponding states relating to a conception leading to a fetal loss.

With this formulation it is also possible to obtain results for the mean and variance of the number of visits to any state, and for the first passage and recurrence times (Feller, 1957; Kemeny and Snell, 1960). Although these derivations are of interest in their own right, they will not be presented here.

NUMERICAL EXAMPLE

Assume that after achieving the size of family they desire, couples resort to a contraceptive which reduces their fecundability (ρ) to .01. Assume further that a pregnancy leading to a live birth takes 9 months and is followed by a postpartum infecundable period of 6 months ($m=15$). If there were no fetal deaths, it can be calculated that the first L conception would occur on the average in the 100th month. The first birth would take place on the average 109 months after the beginning of contraceptive practice. The standard deviation of the intervals is almost 100 months. The mean interval between births would be 114 months (almost 10 years). But, as shown in the first column of Table 1, from the results of Eq. (8)-(11), the probability of avoiding any live births in a 10 year period will be only 33%, with a 25% probability of at least 2 births. If such a contraceptive were used for 15 years, the probability of at least one birth would be 82% and the probability of at least 3 births, 17%.

The effect of two levels of fetal death in such a model is shown in the next two columns of Table 1. The mean intervals are increased considerably as occurs especially at low levels of fecundability (Potter, 1963; Sheps, 1964a). A 10% incidence of fetal death adds almost 12 months to the mean interval and a 25% incidence adds another 23 months. The variance of the intervals is increased still more, producing an increase in the coefficient of variation each time.

The probabilities of live births in 10 or 15 years decrease correspondingly. It is, however, noteworthy that even with a 25% incidence of fetal death, and the low level of fecundability postulated, there would be less than a 44% chance of no births in a 10 year period, and less than a 28% chance of this occurring in a 15 year period. There is, in fact, almost a 10% chance that over a 15 year period 3 or more children would be born to a couple even with a fetal loss rate of 25%.

The effect of fetal losses on the mean and variance of the number of live births is also demonstrated in Table 1. In a period of 15 years, the expected number of births would be 1.5, 1.4 and 1.2 respectively in the 3 cases cited. That the variance would be considerable is seen from the coefficients of variation shown.

The monthly fertility approaches the reciprocal of the mean interval between births (this follows directly from renewal theory or the Markov Chain approach). It may therefore be calculated that the annual fertility rate, to the couples in question, would approach 105, 96 and 81 per 1000 women in the 3 cases illustrated.

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We should like to express our appreciation of the competence, patience and good nature of our typists, Arlene Crossan and Mary Ann

TABLE 1

*Numerical example, with fecundability = 0.01 and
infecundable period of 6 months postpartum **

	FETAL MORTALITY (PERCENT)		
	0	10%	25%
Mean number of months between LB	114.0	125.6	148.7
Variance of intervals	9900	12,345	18,009
C. V. of interval	87%	88%	90%
<i>10 year period</i>			
Probability of:			
0 births	.3277	.3680	.4372
At least 1 birth	.6723	.6319	.5628
At least 2 births	.2531	.2162	.1626
At least 3 births	.0509	.0390	.0243
At least 4 births	.0052	.0035	.0018
At least 5 births	.0002	.0001	.0001
Mean number	0.9818	0.8908	0.7515
Variance	0.7608	0.7090	0.6202
C. V.	89%	94%	127%
<i>15 year period</i>			
Probability of:			
0 births	.1793	.2144	.2796
At least 1 birth	.8207	.7856	.7204
At least 2 births	.4662	.4114	.3253
At least 3 births	.1731	.1380	.0914
At least 4 births	.0412	.0294	.0161
At least 5 births	.0062	.0039	.0018
At least 6 births	.0006	.0003	.0001
Mean	1.5080	1.3686	1.2156
Variance	1.1616	1.0817	0.9489
C. V.	71%	76%	80%

* Total mean duration of infecundable period associated with fetal wastage (including pregnancy) 5 months.

Scully. The calculations presented were obtained in part from a computer program written with the assistance of Arthur LeGasse. Many additional calculations forming a necessary background of the paper were performed by Helen Chun.

SUMMARY AND ABSTRACT

A simplified model is presented for the sequence of events occurring during human reproduction. Like the more general system (Perrin and Sheps, 1964) of which this is a special case, the model provides for fetal wastage and for nonsusceptible periods associated with pregnancy that vary with the outcome of pregnancy. If it is assumed that these periods are of constant duration for each outcome, closed expressions are available for the probability distribution of births in a period of y years after marriage. Numerical values may be obtained from tables of the binomial or Poisson distributions or from a computer program. The model yields generating functions for intervals between births and from marriage until the r -th birth. It is easily extended to provide for complete sterility in part of the population, and (under suitable assumptions) for a distribution of fecundabilities in the population.

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