Mechanisms for the Association of Maternal Age, Parity, and Birth Spacing With Infant Health

John G. Haaga
The research described in this report was supported by the Rockefeller Foundation.

This Note contains an offprint of RAND research originally published in a journal or book. The text is reproduced here, with permission of the original publisher.

The RAND Publication Series: The Report is the principal publication documenting and transmitting RAND's major research findings and final research results. The RAND Note reports other outputs of sponsored research for general distribution. Publications of RAND do not necessarily reflect the opinions or policies of the sponsors of RAND research.

Published 1991 by RAND
1700 Main Street, P.O. Box 2138, Santa Monica, CA 90407-2138
N-2991-RF

Mechanisms for the Association of Maternal Age, Parity, and Birth Spacing With Infant Health

John G. Haaga

Supported by the Rockefeller Foundation
SUMMARY

This Note reviews biomedical mechanisms connecting maternal age, parity, and birthspacing with infant mortality and assesses their likely importance in developing countries. This is partly to help refine estimates of the effects of family planning programs on infant health and partly to identify promising leads for research and the design and targeting of future maternal and child health interventions.

The evidence is strong that young maternal age and primiparity affect infant health via pregnancy-induced hypertension (PIH), intra-uterine growth retardation, and placental malaria. All three are associated with primiparity more strongly than with young maternal age per se. The evidence that young mother’s own linear growth requirements lessen nutrient availability for fetal growth is weak.

Young mothers tend in both rich and poor countries to include disproportionate numbers of the poorest and least educated women. Family planning programs could improve infant health by lowering the percentage of births to adolescents. Insofar as the programs reach poor and uneducated women they allow women to postpone births until they were able to support more children. If family planning is introduced as part of a general extension of maternal and child health services, then the excess risk associated with primiparity for most women in poor countries should be reduced as part of the same process. In poor countries childbearing typically continues into older maternal ages, and grand multiparity is common.

The literature on “maternal depletion” in poor countries is inconclusive. The best established association is between high parity and the prevalence of iron-deficiency anemia, which in turn is associated with prematurity. There is some evidence from severely malnourished communities that successively higher-parity babies are smaller at birth, but it is hard to account for this by gross maternal undernutrition. The apparent energy cost of reproduction is not great enough to account for large birthweight deficits. The association of high parity and low birthweight is most likely a problem of closely spaced pregnancies.

The medical evidence is stronger for an effect of older maternal age on congenital abnormalities associated with chromosomal damage. But congenital abnormalities are relatively minor causes of infant death in poor countries. The direct impact of family planning programs on infant health is most likely to come about through a decrease in the number of exceptionally short intervals. Unfortunately, little is known about how short
intervals put infants at high risk, and thus about the degree to which longer intervals by themselves would reduce risk.

The association of short intervals with low birthweight and infant mortality is only in part a sort of statistical artifact (short intervals include more of the infants born, for various reasons, after short gestation). More important, in all likelihood, is a true causal chain. The best evidence is for some mechanism interfering with the development in early pregnancy of the uteroplacental circulatory system, leading to fetal growth retardation. There may also be problems with reproductive tissues, e.g., cervical incompetence leading to premature delivery. Inadequate recuperation from the first parturition may leave reproductive structures too weak to support the next pregnancy. The WFS studies have found short intervals associated with an excess risk that continued well past early infancy. This is consistent with both prematurity and fetal growth retardation as causal mechanisms.

A high priority for further research should be the collection of information on birthweights, gestational age, and causes of death, in association with data on pregnancy intervals (preferably entire reproductive histories).
ACKNOWLEDGEMENTS

This Note was prepared as a background paper for the Working Group on the Health Consequences of Contraceptive Use and Controlled Fertility of the National Academy of Sciences Committee on Population. Funding was provided in part by grant number GA PS 8813; GA HS 8837 from the Rockefeller Foundation and by grant number R01 HD20029 from the National Institute of Child Health and Human Development.

I received very helpful advice, comments, and references from many members of the Working Group and from others who reviewed earlier drafts of this paper. I would particularly like to thank Julie DaVanzo, Peter Donaldson, Judith Fortney, Ronald Gray, Jorge Martinez Manatou, Anne Pebley, Joseph Potter and James Trussell. None of them should be assumed to agree with the conclusions presented here, however, and none are responsible for the errors that remain.
Mechanisms for the Association of Maternal Age, Parity, and Birth Spacing With Infant Health

John G. Haaga

INTRODUCTION

Overview

This paper reviews possible biomedical mechanisms connecting maternal age, parity, and birth spacing with infant mortality and assesses their likely importance in accounting for the strength of these relationships as observed in household surveys in developing countries. This is partly to help refine estimates of the effects of family planning programs on infant health and partly to identify promising leads for research and the design and targeting of future maternal and child health interventions.

In a review of studies using data from the World Fertility Survey (WFS), Samuel Preston termed maternal age, parity, and birth spacing the "bio-demographic variables" affecting the risk of infant mortality (Preston, 1985, p. 265). Older studies using survey data and, to a lesser extent, data from vital events registration systems had shown excess risks for infants born to very young and very old mothers, for first births and for infants at very high birth orders, and for infants born after (and sometimes before) very short interpregnancy intervals. In the last decade or so analyses of demographic data, notably the WFS and similar retrospective surveys in developing countries, using methods designed to over-

come at least some of the methodological problems, have brought these risk factors into new prominence. "Certainly the most surprising and probably the most important new finding from the WFS," as Preston (1983) puts it, "concerns the exceptionally high mortality rates among children born after a short birth interval" (p. 266).

Family planning programs can affect the distribution of all three of these risk factors in the population and may thereby be an important tool in reducing infant mortality rates. But the causal chains connecting family planning with the ultimate outcome of life or death for an infant are long and complex. "Young mother," "high parity," and "short interval" are not proximate causes of death such as would be listed on a death certificate. Insofar as the associations observed in demographic data are causal and not simply the result of confounding with other social or biological factors, it must be because the biodemographic factors increase the prevalence or severity of other conditions that are the more proximate causes of death. This paper reviews the evidence for some of the more likely mechanisms.

Even in low-mortality countries the large population-based studies that have provided most of our knowledge about the risks associated with these maternal factors (e.g., the Collaborative Perinatal Survey in the United States and the British Perinatal Study) have not been analyzed in a way that would show which direct causes of death are associated with the higher mortality rates for children born to very young and very old mothers and those born at high parity and after very short intervals. The WFS did not collect any information on causes of death. So for this paper most of the evidence about direct causes of death comes from small clinical studies or special-purpose population studies, and their results do not readily or entirely explain the mortality differentials associated with the indirect factors that were measured in the demographic surveys.

None of the causal chains linking maternal characteristics with more direct risk factors and ultimately to poor pregnancy outcomes and infant deaths is entirely understood at the organ system or cellular level. For example, one can observe relationships between anemia or certain maternal infections and premature onset of labor, but it is not known what triggers labor or exactly how these maternal conditions affect the process. And the associations for which the evidence is strongest and the relative risks highest (notably the link between older maternal age and chromosomal abnormalities) are less important as causes of infant death in poor countries than in rich ones. A large part of the work for this paper consisted of culling results from obstetric, biological, and epidemiologic studies in rich countries and guessing their public health significance for poor countries.
There have been a few good longitudinal field studies following infants from before birth in developing countries. But the logistical problems of maintaining a study group and obtaining accurate measurements and cause-of-death reporting preclude large samples. There are some interesting hospital-based studies, but these are always subject to severe selection and ascertainment biases in environments where most mothers and children do not get adequate care.

The remainder of this section discusses in more detail the differences between high- and low-mortality countries in the causes of infant deaths, which have a large influence on my subjective estimates of the likely importance of the causal mechanisms outlined in the rest of the paper. Next I list the possible causal mechanisms for which there is some evidence of association with young maternal age and primiparity. Then I discuss mechanisms that may link old maternal age and high parity with infant health. Finally, possible mechanisms for the effect of short interpregnancy or interbirth intervals on infant health are discussed.

To avoid repetition, maternal nutrition and infectious diseases are discussed only briefly in the second and third sections, which deal with maternal age and parity. They are dealt with more fully in the fourth section, on the effects of short intervals between pregnancies, for which their relevance is judged to be greater.

**Causes of Infant Deaths**

The pregnancy conditions for which evidence of an association with biodemographic variables is strong are not usually very important as causes of infant deaths in poor countries. Conversely, the major proximate causes of infant deaths in poor countries are not clearly related to biodemographic variables.

The causes of infant deaths differ between high- and low-mortality environments. It is difficult to obtain accurate information on causes of death when, as in most high-mortality countries, the majority of deaths are not attended by trained health workers. Even in low-mortality countries where most deaths occur in hospitals and there are strict requirements for certification, recording of causes can be unreliable and it can be difficult even to decide what is meant by cause of death in most situations, if a single cause must be chosen and recorded. But there is a reasonably clear picture of differences between high- and low-mortality countries, at least when causes of death are grouped into very broad categories.

Table 1 presents data on the causes of infant deaths in two reasonably well documented cases, corresponding to high- and low-mortality environments: (1) Recife, Brazil, in the late 1960s, when a special effort was made as part of the Inter-American Investigation of Mortality in Childhood to notify medical authorities and gather information on infant deaths as soon as possible after their occurrence and (2) the United States in 1983. Infectious and parasitic diseases account for a much larger proportion of the total when infant mortality rates are high. The lower the overall infant mortality rate is, the higher the proportion of
TABLE 1 Percentage of Infant Deaths by Cause: Recife, Brazil, and United States

<table>
<thead>
<tr>
<th></th>
<th>Recife, Brazil 1968-1971*</th>
<th>United States 1983</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infectious and parasitic diseases</td>
<td>51</td>
<td>2</td>
</tr>
<tr>
<td>Diseases of the respiratory system</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>Congenital anomalies</td>
<td>4</td>
<td>21</td>
</tr>
<tr>
<td>Certain perinatal conditions</td>
<td>26</td>
<td>47</td>
</tr>
<tr>
<td>Ill defined</td>
<td>8</td>
<td>14</td>
</tr>
<tr>
<td>All other</td>
<td>—</td>
<td>11</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Infant mortality rate per 1,000 live births</td>
<td>91</td>
<td>11</td>
</tr>
</tbody>
</table>

* "Basic causes" only (from Inter-American Investigation of Mortality in Childhood).


deads attributable to congenital anomalies and to "certain conditions originating in the perinatal period," including birth trauma, hypoxia, and "immaturity." And of the deaths due to these conditions, it is likely that a higher proportion of those in poor countries are attributable to poor obstetric care than to the age- and parity-related causes predominant in rich countries. For example, in the Narangwal study in the Punjab, 9 of the 24 deaths ascribed to "intrauterine asphyxia" were associated with administration of pycocin by indigenous practitioners to speed up labor (Kielmann and Associates, 1983, p. 197).

This contrast is important in the present context because it indicates the relative size of the effects that would have to be present for a particular category of cause of death to account for the observed indirect relationships between biodemographic variables and infant mortality. For example, if the effect of a short birth interval is associated with a relative mortality risk of 1.5 (relative to standard risk of 1.0 for births occurring after intervals of 2 to 4 years), and if this association is entirely causal and operates through only one of the categories of cause shown in Table 1 (an artificial and unlikely assumption), then a short birth interval would have to raise the risk of death from infectious and parasitic

2The figures shown in Table 1 are percentages of deaths corresponding to very different levels of infant mortality, of course. The mortality rate due to congenital abnormalities in Recife (4 percent of 91 per 1,000, or just under 4 deaths per 1,000 births) was higher than the same rate in the United States (21 percent of 11 deaths per 1,000, or just over 2 deaths per 1,000 births).
diseases by a factor of about 2. But a short birth interval would have to raise the risk of death from congenital anomalies by a factor of about 50 to account for the whole indirect association between short intervals and infant mortality. This alone makes it more likely that increased susceptibility to infectious disease, rather than increased incidence of congenital anomalies, is the most important underlying cause for the associations between biodemographic variables and infant mortality.

**Low Birthweight and Prematurity**

Low birthweight is associated with a higher risk of infant mortality, morbidity, and developmental problems (IOM, 1985). Infants may be small because they were born at less than full term (before the thirty-seventh week of pregnancy, counted from last menstruation, is a commonly used cutoff) or because they were born at full term after poor growth during uterine life (intrauterine growth retardation, or IUGR). Different combinations of gestational age and weight at birth are associated with different levels of risk to the infant.

Low birthweight and prematurity have many causes, and it is likely that the risk posed by a given deficit varies according to what caused it. The sections that follow discuss the limited evidence relating various biodemographic factors to birthweight and prematurity.

In relative terms, prematurity\(^3\) accounts for a larger proportion of low birthweight infants in rich countries than in poor countries, where many more infants born at term are low in weight (Villar and Belizan, 1982). The relative risk of infant mortality is much higher for the preterm than for the term-but-low-weight infant. This point was brought out very starkly by a recent study of hospital births in Mexico City and Santa Cruz, Bolivia: the risk of neonatal mortality for preterm babies (relative to babies born at term and weighing more than 2,500 grams) was 24 and 100, respectively, in the two sites, compared to relative risks of 4.0 and 3.3, respectively, for babies born at term but weighing less than 2,500 grams (Haas et al., 1987). But the etiology of prematurity is still largely a mystery (Alger and Pupkin, 1986). In an interesting exercise in ascribing the attributable risk of low birthweight and prematurity, and the relative risk in rich compared with poor countries, among different proximate determinants, Kramer (1987) found that only about a quarter of variation in prematurity could be "explained" and much of that was with relatively uninformative determinants such as "nonwhite race."

\(^3\) I use the term *prematurity* and the adjective *preterm* only to mean early labor and delivery, usually defined with a cutoff of 37 weeks' gestation, counted from last menstruation. In older literature *prematurity* was often used for any low birthweight.
YOUNG MATERNAL AGE AND PRIMIPARITY

Effects on Birthweight and Prematurity

In the United States infants born to young mothers are at increased risk of premature delivery, low birthweight, prematurity, and perinatal death. Table 2 shows the relative risks of (1) birthweight less than 2,500 grams and (2) 5-minute Apgar scores (a composite index, including several signs associated with prematurity) less than 7 by mother's age for infants born in the United States in 1983. It can be seen that the risks of poor pregnancy outcomes are higher for younger mothers and that they are especially high among mothers less than 15 years old.

In high-mortality countries as well, infants born to young mothers are often at a disadvantage. In five of the Latin American project sites for the Inter-American Investigation of Mortality in Early Childhood in 1967–1970, infants born to mothers less than 20 years old were between 1.3 and 1.9 times as likely to die in the neonatal period as those born to mothers aged 20 to 24, and their relative risk was about as large for postneonatal deaths as well (Puffer and Serrano, 1973, Table 147). This was entirely associated with age, not primiparity, since a more detailed analysis showed that within mother's age categories first-parity births had the lowest neonatal death rates of all parities in most of the sites (Puffer and Serrano, 1975).

A more common finding is that primiparity is a risk factor for poor pregnancy outcomes over and above the effects of maternal age. The Collaborative Perinatal Study in the United States found that average birthweights were lowest for first births for both black and white infants born in 15 university-affiliated medical

<table>
<thead>
<tr>
<th>Mother's Age (years)</th>
<th>BW &lt; 2,500 grams</th>
<th>5-minute Apgar &lt; 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 15</td>
<td>14.5%</td>
<td>4.1%</td>
</tr>
<tr>
<td>15</td>
<td>12.0</td>
<td>3.2</td>
</tr>
<tr>
<td>16</td>
<td>10.7</td>
<td>3.0</td>
</tr>
<tr>
<td>17</td>
<td>10.0</td>
<td>2.8</td>
</tr>
<tr>
<td>18</td>
<td>9.4</td>
<td>2.6</td>
</tr>
<tr>
<td>19</td>
<td>8.4</td>
<td>2.4</td>
</tr>
<tr>
<td>20-24</td>
<td>7.0</td>
<td>2.0</td>
</tr>
</tbody>
</table>

centers in the years 1959–1965 (Table 3). Perinatal death rates (late fetal deaths plus deaths in the first week of life) were higher for first pregnancies than for second ones, although they tended to increase thereafter with parity. Neonatal death rates tended to increase, although not necessarily monotonically, with parity (Niswander and Gordon, 1972).

By contrast, in data from developing countries, first births do not consistently appear at a disadvantage. In a review of results of the WFS, Preston (1985) found the evidence for an excess mortality risk for first births equivocal. He suggested that in retrospective surveys women may tend to underreport first births of children who later died. The Inter-American Investigation of Mortality in Childhood, in which data were collected shortly after the time of death (and thus presumably would have been less subject to the type of recall bias Preston suggests), found that first births had the lowest mortality rates, within categories of mother’s age, in the four project sites for which data were disaggregated—Chile, Mexico, Canada, and the United States (Puffer and Serrano, 1973, Table 151).

Mojarro and Aznar (1986) present infant mortality rates from rural Mexico by mother’s age and parity (Table 4). They show that the excess risk for infants born to mothers less than 20 years old was for the second and third infants. Presumably a relatively high proportion of these babies are born after a relatively short birth interval and/or after a short gestation (a woman who gives birth for the first time at age 16 does not have enough time to have her third child before age 20, if she is to have the low-risk 2-year interval between births). In these data, infant mortality was actually higher for first-parity births to mothers aged 20 to 24 than for mothers less than 20. But the studies from rich countries showing the excess risk for the “older primipara” usually use the 20- to 24-year-old mothers as the refer-

<table>
<thead>
<tr>
<th>Parity</th>
<th>Mean Birthweight (grams)</th>
<th>Perinatal death ratios</th>
<th>Neonatal death rates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Whites</td>
<td>Blacks</td>
<td>Whites</td>
</tr>
<tr>
<td>0</td>
<td>3,234</td>
<td>2,960</td>
<td>29</td>
</tr>
<tr>
<td>1</td>
<td>3,290</td>
<td>3,029</td>
<td>26</td>
</tr>
<tr>
<td>2</td>
<td>3,288</td>
<td>3,074</td>
<td>40</td>
</tr>
<tr>
<td>3</td>
<td>3,291</td>
<td>3,097</td>
<td>44</td>
</tr>
<tr>
<td>4</td>
<td>3,306</td>
<td>3,107</td>
<td>52</td>
</tr>
<tr>
<td>5+</td>
<td>3,340</td>
<td>3,138</td>
<td>61</td>
</tr>
</tbody>
</table>

Source: Niswander and Gordon (1972).
TABLE 4 Infant Mortality Rates by Parity and Mother’s Age, Rural Mexico, 1965-1974

<table>
<thead>
<tr>
<th>Mother’s Age</th>
<th>Parity</th>
<th>2-3</th>
<th>4-6</th>
<th>7+</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 20</td>
<td>69</td>
<td>106</td>
<td>*</td>
<td>*</td>
<td>86</td>
</tr>
<tr>
<td>20-24</td>
<td>108</td>
<td>65</td>
<td>101</td>
<td>*</td>
<td>83</td>
</tr>
<tr>
<td>25-29</td>
<td>*</td>
<td>56</td>
<td>75</td>
<td>84</td>
<td>72</td>
</tr>
<tr>
<td>30-34</td>
<td>*</td>
<td>*</td>
<td>75</td>
<td>79</td>
<td>77</td>
</tr>
<tr>
<td>35</td>
<td>*</td>
<td>*</td>
<td>99</td>
<td>100</td>
<td>101</td>
</tr>
<tr>
<td>Total</td>
<td>84</td>
<td>74</td>
<td>84</td>
<td>89</td>
<td>83</td>
</tr>
</tbody>
</table>

Note: n = 551 infant deaths, 6,640 live births.
*Fewer than 10 deaths in cell.

Source: Mojarro and Azmer (1986, Table 8.3).

ence group with optimum conditions for childbearing. I suspect that the 20- to 24-year-old primiparae represented in the rural Mexican data include a large number of women who had prior miscarriages. The lowest infant mortality rates in this high-fertility population, in fact, are found along the diagonal of the table: these represent the women who are having the “right” number of live births for their age group.

Some of this difficulty could be removed if data were always available that separated the effects of parity (number of prior live births from gravidity (number of prior pregnancies), but fetal losses are underrepresented in both survey and certificate data, especially in high-mortality countries. The difference between the American and Mexican maternal age comparisons illustrates an important difficulty in making comparisons across populations of the effects of biodemographic variables on infant mortality. Since there are no random controlled trials (one cannot assign women to different parities at different ages), powerful social influences on the timing and pace of childbearing cause selectivity biases that are only partially and imperfectly controlled by the socioeconomic-status variables usually available. The biases vary among societies in magnitude and even direction.

It is difficult to separate in analyses the pure effects of young maternal age and primiparity from the effects on infant health of other factors associated with young motherhood and first parity in different societies. Especially in high-fertility countries, primiparous women are an increasingly select group in each older age group: women in their thirties giving birth for the first time have often had one or more previous pregnancies terminated by miscarriage or induced abortion. (A similar situation exists in sorting out the effects of old maternal age and “grand multiparity,” though there is more variation at the end than at the
beginning of reproductive careers, and the sample size, collinearity, and selectivity problems for statisticians are somewhat more tractable.) For the purposes of this review, the distinction between effects of young motherhood and effects of primiparity is quite important. Family planning programs can be expected to reduce the incidence of births to young women. But the proportion of all births in a population that are first births would likely increase as a result of widespread use of contraception to limit family size (Bongaarts, 1987).

Young maternal age is also confounded by environmental and possibly genetic characteristics that can affect infant health independently. In the United States, for example, young mothers are disproportionately black, poor, unmarried, and uneducated. They are less likely to receive antenatal care early in pregnancy than are older mothers, and the care they do get is often disjointed. Three recent reviews of the literature on the health consequences of adolescent pregnancy in the United States have all come to very similar conclusions (Strobino, 1987; Geronimus, 1987; McAnarney, 1987). As Strobino (1987) puts it, “adolescence, per se, may not be a risk factor for poor health outcomes of the mother or her offspring, but rather . . . the preponderance of other risk factors such as low socioeconomic status, poor prenatal care and primiparity is the reason for their poor outcomes” (p. 111).

To some extent this conclusion also holds for high-mortality countries, even though adolescent childbearing is not such a deviant behavior elsewhere as it is in the United States. Barros et al. (1987a, 1987b), for example, found higher rates of both perinatal and neonatal mortality among infants born to mothers less than 20 years old in a small city of southern Brazil. The mortality differences between these infants and those of mothers aged 20 to 29 completely disappeared when family income and whether the woman received antenatal care were controlled. DaVanzo et al. (1984), using recall data from a household survey in Malaysia, found that first births weighed significantly less than higher-order births. They found a positive bivariate association between mother’s age (up to 35 years) and birthweight. The association between first-birth order and low birthweight persisted in a multivariate analysis controlling for family income and other social characteristics, while the association between young maternal age and low birthweight disappeared in the multivariate analysis. In an analysis of determinants of infant mortality using the same data, younger maternal age (below 18 years) was associated with increased risk of infant death, but the association was much diminished when social characteristics and behavioral variables (notably breastfeeding) were controlled (DaVanzo et al., 1983).

The results of these Brazilian and Malaysian analyses tend to support the conclusion that young maternal age is less important than primiparity as a risk factor for low birthweight and infant mortality. It may be that very young maternal (gynecologic) age poses great risks to the infant, but in the studies reviewed for this paper the age cutoffs used to define young maternal age were sufficiently high that the excess (relative) risk was small. Small sample sizes in population-based studies typically preclude estimation of infant mortality risks
for very young mothers, which means that this potential risk factor is not a major attributable risk for infant mortality in the countries for which we have good information.

The remainder of this section examines in turn the major pathways or proximate causes through which young maternal age could be associated with lower birthweight and infant deaths.

**Mother-Fetus Competition for Macronutrients**

It is generally thought that girls are still growing for 4 years after menarche and that the energy cost of a pregnancy during these 4 years must compete with the energy cost of linear growth of the mother (NRC, 1970). In analyzing data from the Collaborative Perinatal Study, Naeye (1983) showed that infants born to very young (10- to 16-year-old) black mothers had low birthweights and lengths, which he suggested could be explained by the "fetal-maternal competition for nutrients." And in an analysis of data on infants of very young black mothers in New Orleans, Cherry et al. (1987) showed that this birthweight and length deficit persisted through infancy into childhood. But other studies have shown that for most girls the linear growth spurt in adolescence takes place well before menarche or during a period of adolescent subfecundity (see McAnarney, 1987, for a review). The energy cost of linear growth is a fairly small percentage of metabolic requirements even for young children, and linear growth is interrupted quickly when there is nutritional stress. In any case, as discussed further later in this paper, the energy costs of pregnancy are surprisingly low and can usually be met at the expense of maternal fat deposition even during nonharvesting seasons in very poor communities in West Africa.

On the face of it there appears to be little reason to think that absolute shortages of macronutrients are a binding constraint on fetal growth except in the most extreme circumstances. McAnarney (1987) suggests that the small size of the infants born to very young mothers in the United States is more likely due to the mother’s small size at maturity, before pregnancy, and to their greater rates of infection and premature delivery than to a simple competition between two growing children, one in the womb of the other. It may also be that the problems are not so much with the quantity of nutrients in the mother’s circulatory system as with the size and development of the uterine blood vessels early in pregnancy: a fetus can be undernourished even when there are “enough” nutrients around if the maternal-fetal transfer is impaired.4

The situation may be different in poor countries. Age at menarche occurs later

---

4 I discuss this point further below in discussing short spacing between pregnancies. This point has been made in connection with studies of placenta morphology and IUGR in general, but my connection of it to the specific problem of adolescent pregnancy does not have any other support in the literature.
on average in poor countries than in Northwest Europe and North America, where secular declines in age at menarche have been documented. At the same chronological age, teenagers in poor countries are usually at a younger gynecologic age than their contemporaries in rich countries. Growth may last longer after menarche as well.5

My tentative conclusion is that the evidence is weak for an effect of young maternal age on fetal growth and infant health through direct competition for nutrients. More plausible is an association caused by the connection of both very young maternal age and poor infant health with poverty and poor sanitary conditions. There is little evidence directly bearing on the issue of young mothers, but it could also be that "uteroplacental perfusion" of nutrients is impaired in very young women, as it appears to be in animal studies of undernutrition in pregnancy.

**Micronutrient Deficiencies**

Iron and folate deficiencies are common in pregnancy, and routine supplementation is recommended by the World Health Organization (WHO). In the United States, teenage mothers are often found to be more anemic than older mothers, but this effect is most likely due to their poverty and poor diets rather than to any true age effect (Strobin, 1987). The more common finding in poor countries appears to be an association of iron and folate deficiencies in high-parity pregnancies (anemia is discussed in greater detail later in this paper.

Zinc is a micronutrient that has attracted a great deal of attention in recent research (Swanson and King, 1987). It is suspected that one of the ways in which maternal smoking and alcohol intake affect fetal growth is by interfering with the mother's zinc utilization. Whether because of these behaviors or because of dietary deficiencies, low circulating zinc levels have been found in pregnant teenagers in the United States. Pregnancy-induced hypertension and poor pregnancy outcomes (e.g., prematurity, IUGR, congenital malformations) have been associated in observational studies with low circulating zinc levels, but so far results of supplementation trials are equivocal. Apparently the assessment of zinc status is extremely difficult, and the studies reviewed by Swanson and King have all been conducted in low-mortality countries. For the purposes of this paper, zinc deficiency must be considered a factor that may prove an important link between

---

5This is at least a possibility. It is known that children in poor communities, where undernutrition and infectious diseases are prevalent, are shorter than those of similar genetic background who have had less stress, at least until the age of 7 or so. But adults in poor countries (e.g., West Africa) are not much smaller than those from rich countries. It has been suggested that linear growth lasts longer (say, into the early twenties) to account for this discrepancy (Habicht et al., 1974). This might prolong the period between menarche and the end of linear growth.
biodemographic risk factors and infant health in developing countries, but there is virtually no evidence yet.

Infections

Infections of the urinary tract are associated with premature delivery and neonatal sepsis.\(^6\) I have found no studies showing differences by age and parity in maternal or fetal susceptibility to infections, which leaves differences in exposure as a likely mechanism. Young mothers may be more likely than older ones to have sexually transmitted diseases (STDs) and other genito-urinary infections. Presumably because in many countries young mothers are a select group, with lower social and economic status and perhaps with more sexual partners than much older women.

Congenital syphilis was an important cause of perinatal mortality in one urban African sample (Naeye et al., 1977). Efiong and Banjoka (1975) found syphilis in 7 out of 95 primigravidae less than 16 years old in urban Nigeria, compared to none in 100 older primigravidae selected as controls. A prospective study in Sierra Leone found that pregnant women under age 20 were more likely to have both urinary and genital tract infections in pregnancy than were older pregnant women (WHO, Family Health Division, 1981).

Pregnancy-Induced Hypertension

Pregnancy-induced hypertension (PIH) is associated with premature delivery and placental abruption, both of which are associated with low birthweight (Niswander, 1977).\(^7\) In the 1958 British Perinatal Mortality Study it was found that 18 percent of infants born to mothers diagnosed as having pre-eclampsia (PIH and edema) weighed less than 2,500 grams at birth, compared to 5.4 percent of the infants born to normotensive women, and that 8.5 percent of the deliveries following a diagnosis of pre-eclampsia took place before 37 weeks of gestation, compared to 5.1 percent of deliveries for the normotensive women (Alberman, 1984). Undetected PIH can progress to the convulsions of eclampsia, putting both the pregnant woman and her unborn child at very severe risk of death. Even among women diagnosed as having toxemia, or pre-eclampsia, who are under good obstetric care and who do not progress to eclampsia, the risk of perinatal mortality is elevated—double in one study in the United States in the 1970s (cited by Davies and Dunlop, 1983, p. 201).

The precise etiology of PIH is unknown, but it is thought to be a reaction of the

---

\(^6\)Other maternal infections are discussed later in this paper.

\(^7\)PIH is the term generally used now in North America. The more common term in Britain is gestational hypertension.
maternal circulatory system to the placenta because the syndrome never appears in nonpregnant women and because it is so powerfully associated with first pregnancies. About 1 in 20 primigravidae in the United States are diagnosed as having PIH, and the risk of recurrence is fairly high (about a third of those who have it with one pregnancy will get it again); most of the multigravidae with PIH had it in their first pregnancy (Mehta and Young, 1987). The incidence is highest in the United States for poor black women.

Unfortunately, PIH is not easy to diagnose, especially in settings where women do not get medical attention early and often during their pregnancies. Older women and black women in the United States have higher rates of underlying ("essential") hypertension, which poses little risk. Many women have a drop in blood pressure in early pregnancy followed by a rise back to their prepregnancy levels; this is often a less serious indication easily be mistaken for PIH (Davies and Dunlop, 1983). It is thus very difficult to estimate the prevalence of PIH in either low- or high-mortality countries.8

In an analysis of data from a referral hospital in Harare, Zimbabwe, Crowther (1986) had multiple blood pressure observations for enough of his subjects to distinguish between essential hypertension (he used the term chronic hypertension) and PIH, the latter being defined as high blood pressure appearing after the twentieth week of gestation in a patient previously normotensive or normotensive after the sixth week postpartum. He also used the presence or absence of proteinuria to diagnose pre-eclampsia (PIH plus proteinuria). About 45 percent of the PIH cases were women less than 20 years of age, compared to 20 percent of the general obstetric population. Among the hypertensives the diagnosis of PIH was more common among those less than 30 years old and the diagnosis of chronic hypertension more common among those over 30 years old. Perinatal mortality was much higher (79 per 1,000 live births) for the hypertensives than for the normotensives (26 per 1,000). Interestingly, the women in Crowther's sample with only PIH (no proteinuria) had perinatal mortality rates comparable to those of the normotensive women; the excess rate for hypertensives was due to higher death rates for infants born to women with pre-eclampsia and chronic hypertension. This underlines the heterogeneity of the "high blood pressure during pregnancy" population. A series of blood pressure readings is important for surveillance, which of course depends on regular antenatal care and good recordkeeping.

Harrison (1985) reports rates of obstetric complications for hospital births in northern Nigeria (Table 5). Among primigravidae the rates of pre-eclampsia were slightly higher for women below age 20, rising again for those over 25 (who accounted for only 7 percent of first births). There was a much starker age

---

8Davies and Dunlop (1983) cite the experience of the Collaborative Perinatal Study in the United States to show that even "first-class departments of obstetrics give contradictory results even with agreed protocols and definitions" (p. 182).
TABLE 5 Rates of Pre-eclampsia and Eclampsia Among Singleton Hospital Births in Northern Nigeria, by Age and Parity

<table>
<thead>
<tr>
<th>Age of Mother</th>
<th>&lt;15</th>
<th>15</th>
<th>16</th>
<th>17-19</th>
<th>20-24</th>
<th>25-29</th>
<th>30+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-eclampsia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primigravidae</td>
<td>11.6</td>
<td>10.4</td>
<td>10.3</td>
<td>10.2</td>
<td>9.9</td>
<td>15.0</td>
<td>12.9</td>
</tr>
<tr>
<td>Multigravidae</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(20-29, parities 1-4 = 3.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(30+, parity 5+ = 5.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eclampsia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primigravidae</td>
<td>16.7</td>
<td>12.8</td>
<td>7.4</td>
<td>4.9</td>
<td>2.7</td>
<td>2.5</td>
<td>.32</td>
</tr>
<tr>
<td>Multigravidae</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(20-29, parities 1-4 = 0.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(30+, parity 5+ = 0.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Source: Adapted from Harrison (1985, Appendix 4.3).

differential in the more serious diagnosis of eclampsia, however: the prevalence of pre-eclampsia in primigravid women less than 15 years old was six times that for primigravid women aged 20 to 24. Ojo and Oronsaye (1988) present data from another hospital-based study in Nigeria, again showing higher rates of pre-eclampsia for younger primigravidae than for those in their twenties (33 percent for women less than 20 years old compared to 21 percent for those aged 20 to 24).

One of the main problems for maternal and child health in this population, according to Harrison (1985), is "the strongly held belief that home delivery is best for all primigravidae, especially the youngest" (p. 91), which may account for the very high rates of eclampsia relative to pre-eclampsia. Lawson and Stewart (1967) similarly observed that PIH is a much more threatening condition for women (and I presume for the infants if their mothers survive) in poor countries because they often present at hospitals only after convulsions have begun. The lack of adequate antenatal care in many places could lead to a detection bias that makes it difficult to interpret statistics based on hospital births: higher rates of pregnancy complications among young women may be due to differences among age groups in the likelihood of an uncomplicated delivery taking place in a hospital as well as to true differences in the prevalence of complications.

Malaria

Malaria is a major public health problem in the tropics. The WHO estimates that there are over 100 million clinical cases (new and recurring) each year. Half the world's population lives in areas covered by antimalarial campaigns, yet the
overall situation has been “static” in recent years (WHO Malaria Action Programme, 1987).
Because of its prevalence, if malarial infestations affect differentially the health of infants born at different parities or to mothers at different ages, then even a fairly small effect could account for a large part of the excess risk attributable to maternal age or parity.

In regions where malaria is relatively rare and where many adult women do not have acquired immunity, or among migrants who did not acquire immunity as children, malaria during pregnancy is devastating for both mother and fetus or neonate. More significant for our purposes is the situation in the large regions of the world, notably in sub-Saharan Africa, where malaria is “endemic”; “Where indigenous adult women have acquired significant protective immunity, the effects of malaria on pregnancy and its outcome are much more difficult to assess” (McGregor, 1984, p. 517).

One theory is that there is a breakdown in acquired immunity during early pregnancy and that maternal immunity is only gradually reacquired in late pregnancy. In any case the placenta appears to be a preferred site for the malaria plasmodium. Brabin (1983) reviewed recent hospital studies in Tanzania and Cote d'Ivoire in which about a third of all placentas were infested by *falciparum* (the most common agent of the infection during pregnancy in Africa). Parasitization of the placenta appears to interfere with the circulation of maternal blood in the spaces between villi, and it is associated with low birthweight, though it is still not clear how much of this effect is due to prematurity and how much to intrauterine growth retardation (Lawson and Stewart, 1967; Brabin, 1983). In 10 studies reviewed by Brabin, infants born to women whose placentas were infected with *falciparum* had birthweights that were on average 50 grams less than those of women whose placentas were free of the parasite.

It is suspected that placental malaria is also associated with greater risk of late fetal death and stillbirth, but “no study has quantified the part it plays in inducing spontaneous abortion, or established a clear and significant relationship between it and enhanced stillbirth rates” (McGregor, 1984, p. 523).

In African studies primigravidae have about double the rate of placental malaria of multigravidae. Bray and Anderson (1979) presented population-based data for 1,000 pregnancies in several Gambian villages, showing that 59 percent of primiparæ were infected during pregnancy, compared with 31 percent of women at parity 4 or more. Neither the causes of the parity difference in infection rates nor its implications for stillbirth rates, infant growth, and infant mortality are clear. Nonetheless, McGregor (1984) reviewed the fragmentary evidence from

---

9Judith Fortney (1988, Family Health International, personal communication) points out that maternal immunity to non-A non-B hepatitis, common in parts of Africa and South Asia, may similarly break down in pregnancy.
Africa showing that placental malaria infestation was not only more common in
primigravidae but also that the associated maternal anemia and birthweight deficit
were larger for primigravidae than multigravidae.

Apparently congenital malaria or febrile attacks in infancy are rare in areas
where malaria is endemic (Lawson and Stewart, 1967; McGregor, 1984). The
effect of malaria during pregnancy is likely to be most pronounced with respect to
stillbirth rates; its effect on infant mortality would be through the increased
susceptibility of the premature and low-birthweight infant to other infections.
Bray and Anderson (1979) reviewed evidence that malarial infection interferes
with the transmission of Immunoglobulin G from the mother to the fetus, so that
"the infant nourished from the infected intervillous spaces of the placenta may,
three months later, be at a disadvantage to malaria parasites" (p. 429); due to
depressed immunocompetence and lower birthweight, such infants may be more
susceptible to bacterial or viral infections as well. I have found no studies that
followed infants born to mothers with infested placentas and assessed their risks of
postnatal morbidity and mortality.

The association of malaria in pregnancy with first parity is the only clear link
between the biodemographic variables of interest here and parasites involving
infants.

Complications of Delivery

Fortney et al. (1986) present evidence from records collected from 86 hospi-
tals, mostly in developing countries, showing that in cases of vaginal delivery of a
breech presentation, the perinatal deaths rates were significantly lower for multi-
para than for primiparae. Obstetric management of breech presentation is
probably more aggressive for primiparae, but of course many of the poorest
women have no access to facilities that can perform a safe caesarean section.
Thus breech presentation may be more common for grand multiparae, but higher
case-mortality rates for primiparae would lead to a parity differential, probably
small, in infant mortality.

Conclusions

The mechanisms through which young maternal age and primiparity can affect
infant health and for which the evidence is strongest are pregnancy-induced
hypertension, intrauterine growth retardation, and placental malaria. All three are
associated with primiparity more strongly than with young maternal age per se.
The evidence that a young mother’s own linear growth requirements lessen
nutrient availability for fetal growth is weak. The disadvantages associated with
young motherhood are primarily those of poverty and ignorance, since young
mothers in both rich and poor countries tend to include disproportionate numbers
of the poorest and least educated women. Young mothers have been found, for
example, in several studies to have higher rates of genital and urinary infections, which can cause prematurity.

There appears to be an interaction between age and primiparity such that first births to older women are at a particular disadvantage. Some of this effect is due to higher rates of chromosomal abnormalities for infants born to women nearing the end of their fertile years. Older primiparous in poor countries are usually a very select group, however, including many women who aborted previous pregnancies, so it is difficult to separate the effects of age from those of fecundity and other woman-specific factors not easily measured in the data available to demographers.

Even if one concludes that the associations between young maternal age and infant mortality are not true age effects, it may still be true that family planning programs could affect infant health by lowering the percentage of births to adolescents. Insofar as the programs reach poor and uneducated women and give them control over their fertility, they would allow women to postpone births until they were able to support more children.

PIH, many maternal infections, and malaria are all conditions that even "low-tech" antenatal care is designed to detect and/or treat. If family planning is introduced as part of a general extension of maternal and child health services, the excess risk associated with primiparity for most women in poor countries should be reduced.

It would be useful to compare the excess mortality risk for first births in regions of malaria endemicity with that in comparably poor but nonmalarious regions. In areas where first births appear to be at greatest disadvantage, more detailed field studies would be indicated. It would be impossible to trace the full course of the postulated mechanisms in a prospective study, since detectable maternal conditions would have to be treated. But field studies would usefully supplement current evidence, most of which is based on hospital data of uncertain selectivity, showing associations of young maternal age and primiparity with preventable diseases in pregnancy.

OLDER MATERNAL AGE AND GRAND MULTIPARITY

Relative Risks of Poor Pregnancy Outcomes and Infant Deaths

Hansen (1986) reviewed studies, mainly from low-mortality countries, of the effects of older maternal age on the health of mother and infant and concluded that "the literature seems to support the finding that older women have increased incidences of babies weighing less than 2,500 grams at birth (probably both preterm and small-for-gestational-age) and babies more than 4,000 grams. This is consistent with the finding of increased rates of hypertension and pre-eclampsia (preterm and SGA) and diabetes (large babies) among older pregnant women" (pp. 731–732). Diabetes is rare enough (and the infant mortality differential
associated with very high birthweight is small enough) that it is unlikely to produce a discernible impact on infant mortality in poor countries. PIH, prematurity, and chromosomal abnormalities (for which infants born at first parity to older mothers are at increased risk) are the more important pathways for this review.

Besides older maternal age per se, grand multiparity has been found to be associated with infant mortality in many studies. Like very young maternal age, very high parity is often a “marker” for low social status and income, since fertility rates are inversely associated with income in societies that have begun the demographic transition. This and a more direct selection effect caused by purposeful efforts to replace children who have died complicate the interpretation of infant mortality rates at high parity.

The British Perinatal Mortality Survey of all pregnancy outcomes in a period during 1958 showed a U-shaped association of rates of both low-birthweight and preterm births with parity (Table 6).

Fortney et al. (1983), in comparing data on deliveries in urban teaching hospitals in Mexico and Egypt, found that the largest association of older maternal age and child survival was for first-parity births (Table 7).\(^{10}\)

These mortality differences were not due to differences among mother’s age groups in the prevalence of low birthweight; in fact, the older primigravidae had a lower incidence of low birthweight than either younger primigravidae or older muligravidae (Fortney et al., 1983, Table 4).

Similarly, in analyzing data for a “natural fertility” religious group in Israel, Seidman et al. (1987) found that stillbirths were more common for grand multiparae (parity 6 and over). This mortality differential was not associated with a parity effect on birthweight, since rates of low birthweight decreased monotonically with parity within sibship groups. The very highest parity (8+) infants in this study had higher rates of low birthweight than lower-parity infants, but Seidman et al. show that this difference is reversed when sibship groups are compared: the high-parity infants weigh more at birth than their older siblings did. They argue that this is evidence of a form of selection, presumably biomedically, since this is an aggressively noncontracepting population. That is, women who have small babies are more likely than others to progress to higher parities.

Bakketeig and Hoffman (1979) demonstrated similar effects using data on singleton births at parity 4 or less plus late fetal deaths in Norway. Perinatal mortality and rates of low birthweight were both larger for first parity outcomes in the marginals for the total sample. But within groups defined by the number of births to the same woman in a 6-year period, both rates fell monotonically with

---

\(^{10}\) I have omitted here the data from Hungary that Fortney et al. present, which did show an association between older maternal age and low birthweight but that also showed much higher survival rates in all groups and no association of maternal age with survival.
TABLE 6 Low Birthweight and Preterm Births by Parity, Britain, 1958

<table>
<thead>
<tr>
<th>Parity</th>
<th>Birthweight &lt; 2,500 grams</th>
<th>Gestation &lt; 37 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>7.6%</td>
<td>4.7%</td>
</tr>
<tr>
<td>1</td>
<td>5.4%</td>
<td>3.9%</td>
</tr>
<tr>
<td>2-3</td>
<td>6.8%</td>
<td>5.2%</td>
</tr>
<tr>
<td>4+</td>
<td>7.4%</td>
<td>5.5%</td>
</tr>
</tbody>
</table>


TABLE 7 Percentage of Neonates Surviving Until Mother’s Discharge from Hospital, by Mother’s Age and Parity, Mexico and Egypt, 1977–1980

<table>
<thead>
<tr>
<th>Mother’s age</th>
<th>Mexico 20-34</th>
<th>35+</th>
<th>Egypt 20-34</th>
<th>35+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>96.7</td>
<td>89.2</td>
<td>96.0</td>
<td>87.5</td>
</tr>
<tr>
<td>1-3</td>
<td>96.6</td>
<td>95.6</td>
<td>95.3</td>
<td>90.5</td>
</tr>
<tr>
<td>4+</td>
<td>94.9</td>
<td>90.3</td>
<td>91.8</td>
<td>87.3</td>
</tr>
</tbody>
</table>

Source: Forney et al. (1983).

parity. Only children were overrepresented in the first parity group, children from two-child families are overrepresented in the first two parities, and so forth. Bakketeg and Hoffman’s results are hard to interpret because they pertain to births during a specified time period (1967–1973), so their large families may consist disproportionately of short-interval births. Also, the replacement effect—intentionally quick conception following a fetal or infant death—is not well controlled in this analysis (though its effects on birthweight should have been negligible).

In the Collaborative Perinatal Study in the United States, higher-parity infants were at much higher risk of death both in the perinatal and neonatal periods (though the neonatal mortality differential associated with parity was much smaller for blacks than for whites) (Niswander and Gordon, 1972; see Table 3 above).

In reviewing the literature mainly from low-mortality countries, Hansen (1986) concluded that “there is an association between age and risk for spontaneous
abortion, but the magnitude of the risk is unclear because of the unknown contribution and/or study bias of the factors of gravidity, birth order, and reduced fecundity" (p. 735).

Interpretation of the cross-sectional associations of age and parity with spontaneous abortion and prematurity is difficult because of the high risk of repeat abortions (Mehta and Young, 1987). Especially in societies in which fertility control is efficient, women who are trying to have babies at older ages and higher parities may disproportionately consist of those who have had previous abortions and stillbirths. Powell-Griner (1987) presented results that distinguish nearly the effects of parity with and without prior pregnancy loss. The data set she used was created by linking birth and infant death records for all births and late fetal deaths (n = 647,953) in eight states in the United States in 1982. Table 8 shows the perinatal death rates for various combinations of parity, birthweight, and prior loss, crude and adjusted for effects of social/demographic variables and adequacy of prenatal care.

In both birthweight categories, perinatal death rates for infants of parities 4 and over were well below those for first-parity infants if no prior loss was reported and well above those for first-parity infants when there was a prior loss. Adjustments for maternal characteristics and adequacy of prenatal care made these differences even starker. For the "no loss" multiparae the adjusted perinatal death rates for parities 4 and over are slightly higher than for parities 2 and 3, though both are far lower than for first-parity infants in either weight category. For the "prior loss" multiparae both crude and adjusted rates are lower in each weight category for parities 4 and over than for parities 2 and 3. Parities 2 and 3 usually appear in the

<table>
<thead>
<tr>
<th>Parity/Prior Loss</th>
<th>Birthweight, 1,500-2,499 grams</th>
<th>Birthweight, 2,500-3,999 grams</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Crude</td>
<td>Adjusted*</td>
</tr>
<tr>
<td>First</td>
<td>39.4</td>
<td>41.1</td>
</tr>
<tr>
<td>2-3, no loss</td>
<td>15.4</td>
<td>1.4</td>
</tr>
<tr>
<td>4+, no loss</td>
<td>11.9</td>
<td>3.6</td>
</tr>
<tr>
<td>2-3, prior loss</td>
<td>94.7</td>
<td>137.0</td>
</tr>
<tr>
<td>4+, prior loss</td>
<td>49.7</td>
<td>63.6</td>
</tr>
</tbody>
</table>

*Adjusted for maternal age, race, education, marital status, and whether or not the mother received adequate prenatal care.

literature to be the safest, so I can suggest only that this last difference is a selection effect: women in the parities 2 and 3 group with prior loss have had a very high proportion of their pregnancies end in fetal death. Those in parity 4 include many women with lower proportions of aborted pregnancies and presumably greater intrinsic ability to bring babies to term. Powell-Griner’s (1987) results show that the excess risk of perinatal death for higher parities in the United States nearly disappears when prior loss is taken into account: the risk is very largely a risk of recurrence.\textsuperscript{11}

Kiely et al. (1986) performed a very useful analysis of certificates for all singleton live births and late fetal deaths in New York City during 1976–1978, separating age and parity effects and mortality in the late fetal period, before and during labor, perinatal deaths attributable to congenital abnormalities, and neonatal deaths for causes other than congenital abnormalities. This is one of the few analyses from any country associating age and parity with cause of death. Kiely et al.’s multivariate analysis controlled for mother’s race, educational attainment, and marital status. Fetal deaths were most strongly associated with maternal age but are less relevant for our purposes because they are theoretically unrelated to the infant mortality differentials we are trying to explain. For intrapartum deaths there was no risk difference by maternal age. Infants born to mothers over 35 were at increased risk for perinatal deaths attributable to congenital abnormalities (relative risk of 1.54 compared with infants born to women aged 25 to 29). For neonatal deaths due to other causes, there was no main effect of high parity nor was there an effect of maternal age for infants of second or higher parity. There was, however, a clear age differential in the risk of neonatal mortality for first-parity infants born to mothers of different ages. First-parity infants born to mothers aged 35 and over had a relative risk of 2.33 (95 percent confidence interval: 1.75–3.09) for neonatal death for causes other than congenital anomalies, compared with 1.43 (1.23–1.68) for first-parity infants born to mothers aged 25 to 29. (In each case the risk is compared with the risk to higher-parity infants born to women aged 25 to 29.) Kiely et al. suggest that better obstetric management of high-risk pregnancies has resulted in more infants of older primiparae surviving for a few days or weeks, albeit in a weakened state. This explanation would not hold for most women in high-mortality countries, who have no access to obstetric and neonatal intensive care.

In a prospective study in rural central Java, Indonesia, effects of maternal age and parity on child mortality at different ages were distinguished (Santow and

\textsuperscript{11}The “high-parity” category in this analysis is of course not very high by world standards. Analyses of data from the United States that use higher cutoffs run into very severe sample size problems (as it was, Powell-Griner used linked certificate data on nearly a quarter of all births in the United States that year) and the selectivity biases noted in the text. This makes “natural fertility” samples like those of Seidman et al. especially valuable.
Primiparity was associated with greater risk of death in early infancy, suggesting prenatal influences, while older maternal age and high parity were associated with greater risk in later infancy and during the second year of life, suggesting causes associated with the postnatal environment. This study had small numbers of deaths, illustrating again the difficulty of combining good measurement of independent variables and realistic field conditions with large samples and statistical tests of high power.

Congenital Abnormalities

All the studies reviewed by Hansen (1986) found an association between older maternal age and chromosomal abnormalities in aborted or stillborn fetuses and congenital abnormalities in live-born infants. The association of advanced maternal age with Down’s syndrome has been known for decades, and more recently it has been linked with other chromosomal abnormalities (Hook, 1985). Maternal age has a “strong, ubiquitous positive association with all viable trisomies [including trisomy 21, which causes Down’s syndrome], and with most that are not viable,” according to Hook (1985, p. 126). Some abnormalities appear to be associated with paternal age as well, but not as strongly as with maternal age. The explanation for the association of maternal age and chromosomal abnormalities is apparently unknown. It is usually ascribed to some biologic aging of the ova. Hook suggests that it may in part be an effect of higher rates of late fertilization of ova due to lower frequency of sexual intercourse among older people.\(^\text{12}\)

Other malformations not attributed to chromosomal abnormalities (e.g., spina bifida, cleft palate) have also been found to be associated with advanced maternal age, but the age gradient is not so steep (and in the case of the more common condition, cleft palate, the case mortality rates are not so severe) as for chromosomal abnormalities (Hansen, 1986).

Iron-Deficiency Anemia and Micronutrient Deficiencies

The main way in which maternal anemia could affect infant health is through an association with premature delivery. Requirements for dietary iron increase greatly during pregnancy, approximately quadrupling in the last trimester when stores are laid down in the fetal liver. Pregnant women are often found to have

\(^{12}\)Frequency of intercourse is usually related more strongly to duration of marriage than to age (with which it is confounded), but I found no studies reporting incidence of congenital abnormalities by marital duration. In any case, distinguishing age from intercourse-frequency effects should be a high priority for epidemiologists if Hook (1985) is right and there really is a possible role for the latter, since the distinction would have practical and important implications for older women contemplating motherhood.
lower hemoglobins than nonpregnant women (Royston, 1982). Anemia is particularly severe in areas where hookworm infestation is common, throughout the wet tropics (Lawson and Stewart, 1967).

Royston (1982) cites one Kenyan study showing a higher prevalence of anemia in young primiparae, but the more common finding has been an association of high parity with iron-deficiency anemia. Data on singleton deliveries at 11 Indonesian teaching hospitals, for example, show an association of mother's hemoglobin in pregnancy with parity and birthweight (Table 9). Women who subsequently gave birth to infants weighing less than 2,500 grams had hemoglobin counts in pregnancy averaging 9.5, compared with 9.9 for women who gave birth to heavier infants.

Multiple Births

Dizygotic twinning is associated with maternal age and parity. Allen (1984) presents multiple birth ratios for all whites born in the United States in 1964 (Table 10). The associations with age and parity appear to be shaped like an inverted U, with peak incidence of multiple births among grand multiparae in their thirties. Why this is so is not known. There are also racial, presumably genetic, differences. Blacks in the United States in every age/parity group have a rate of twinning about 1.5 times that of whites, and rates of twinning among blacks in Africa are even higher (Allen, 1984).

Twins are more likely than singletons to be born prematurely and to be of low weight for gestational age. They also suffer higher infant mortality rates. Multiple births are not common enough to account for a very large part of the risk attributable to maternal age and high parity, but they are included here because

<table>
<thead>
<tr>
<th>Birthweight</th>
<th>&lt;2,500 grams</th>
<th>2,500+ grams</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>9.8</td>
<td>10.1</td>
</tr>
<tr>
<td>2–4</td>
<td>9.4</td>
<td>9.9</td>
</tr>
<tr>
<td>5+</td>
<td>9.1</td>
<td>9.2</td>
</tr>
<tr>
<td>Total</td>
<td>9.5</td>
<td>9.9</td>
</tr>
<tr>
<td>(n = 4,377)</td>
<td></td>
<td>(n = 13,747)</td>
</tr>
</tbody>
</table>

Source: Kessel et al. (1985).
TABLE 10 Twin Pairs per 1,000 Deliveries, by Mother’s Age and Parity, United States, 1964

<table>
<thead>
<tr>
<th>Mother’s age</th>
<th>Parity</th>
<th>?+</th>
</tr>
</thead>
<tbody>
<tr>
<td>15–19</td>
<td>2</td>
<td>—</td>
</tr>
<tr>
<td>20–24</td>
<td>3</td>
<td>—</td>
</tr>
<tr>
<td>25–29</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>30–34</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>35–39</td>
<td>6</td>
<td>11</td>
</tr>
<tr>
<td>40–44</td>
<td>2</td>
<td>5</td>
</tr>
</tbody>
</table>


(Unlike most of the intervening conditions studied here) they should be easy enough to account for in the data usually available for the study of mortality differentials in populations. (Most of the studies showing the association of biodemographic variables with infant mortality exclude multiple births.)

Complications of Delivery

The Collaborative Perinatal Study showed increasing rates of premature rupture of the membranes with maternal age: from 0.8 percent of deliveries for women aged 25 to 29 to 2.1 percent of women aged 40 to 44 (Kane, 1967). Placental abruptions also increased in frequency with maternal age and parity, when cigarette smoking was controlled for in the analysis (Naeye, 1983), perhaps due to the associations with hypertension discussed above.

Conclusions

Most of the studies that have shown excess risks of morbidity and mortality for infants born to older mothers or those at very high parity have used data from countries with low infant mortality rates, mainly in Europe and North America. In these countries increasing numbers of women are delaying childbearing into their thirties and early forties, making the consequences of older maternal age for the infant an important public health concern.

Grand multiparity, by contrast, is now exceedingly rare in these countries. In many poor countries, however, childbearing typically continues, even if it does not start, at older maternal ages, and grand multiparity is not at all uncommon. It is thus important for the design and targeting of maternal and child health and family planning programs to distinguish the effects on infant health of high parity
from those of older maternal age and of maternal age as such from those of primiparity at older ages.

The mechanism for which the evidence is strongest is the effect of older maternal age on congenital abnormalities associated with chromosomal damage. As noted earlier, however, congenital abnormalities are relatively minor causes of infant death in poor countries. The same could be said of complications of labor and malpresentations, at least as direct causes of infant death. It may be that these fetal abnormalities and obstetric complications are important as contributory factors to infant deaths in poor countries, even when they do not show up as proximate causes of death. For example, for every perinatal death directly due to these causes, there may be many more infants who survive but who are weak and excessively susceptible to infectious diseases later in infancy.

The risk of pregnancy-induced hypertension rises rapidly with age for primigravidae but and less severely for multigravidae. Older primiparae are a smaller group in poor countries than in rich ones, and they include many women who have had difficulty getting pregnant or who have had prior spontaneous abortions. The extensive literature on risks to the older primiparae deals almost exclusively with low-mortality countries, although the study from central Java discussed above suggests that infants of older primiparae are clearly at high risk in poor countries as well.

The literature on "maternal depletion" in poor countries is inconclusive. (An excellent review can be found in Costello, 1986.) The best established association is between high parity and the prevalence of iron-deficiency anemia, which in turn is associated with prematurity. There is some evidence from severely malnourished communities that successively higher-parity babies are smaller at birth, but it is hard to account for this by gross maternal undernutrition. The apparent energy cost of reproduction is not great enough to account for much of a birthweight deficit. The association of high parity and low birthweight is most likely a problem of closely spaced pregnancies and is discussed further in the next section.

Most high-mortality countries do not have vital statistics reporting systems that are as complete as or that contain such detailed information as that used by Powell-Grimmer (1987) for the analysis discussed above. Separating the risk associated with high parity (and old maternal age) into "recurrence risk" versus "true parity and age effects" would require longitudinal data on women's reproductive careers. Such data would probably have to be gathered prospectively, since spontaneous abortions are subject to severe underreporting in retrospective self-report data, much more so than infant deaths. And prospective samples are very hard to maintain in sizes large enough to guarantee enough fetal losses and infant deaths for separate analysis by parities.

This is an important limitation of available research for the purposes of this review. The effect of family planning programs on infant mortality rates through reduced numbers of births to older women and high-parity births would presuma-
bly only operate on "unwanted" births. Women who are consciously trying to have babies in order to make up for earlier losses are unlikely to use contraception. The effect of increased contraception on perinatal death rates (and presumably neonatal death rates as well) will not be commensurate with the reduction in the proportion of births that are at high parity.

EFFECTS OF SHORT INTERVALS BETWEEN PREGNANCIES

Many studies from developing countries have found an association between the length of the preceding birth (or pregnancy) interval and the risk of infant death for the second child of the pair. Less commonly an association has been found with the risk for the first child of the pair. Mojarro and Aznar (1986), for example, found a U-shaped relationship between length of the preceding interval between births and infant mortality rates in rural Mexico, with rates declining as intervals increased and then rising again after intervals of 4 years (Table 11). Both neonatal and postneonatal infant mortality rates were higher for the shorter intervals: infants born 12 to 23 months after a live birth had neonatal mortality rates 1.6 times as high, and postneonatal mortality rates 1.5 times as high, as for infants born 24 to 35 months after a live birth. They also examined the association between short preceding birth interval and infant mortality, stratifying by age of the mother. There were very few deaths in each age/interval category for their shortest category for birth intervals (8 to 11 months), but the relative (not the absolute) risk for the 12- to 23-month intervals compared with 24+ months appeared to decline somewhat for women over 30.

It is exceptionally difficult to sort out the direction of causation and to estimate the size of effects in these relationships between pregnancy intervals and infant mortality. [Preston (1985) discusses some of the sources of confounding.] The excess mortality of those born after a short interval may merely reflect the fact

<table>
<thead>
<tr>
<th>Interval Between Live Births (months)</th>
<th>Infant Deaths (per 1,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8-11</td>
<td>168</td>
</tr>
<tr>
<td>12-23</td>
<td>102</td>
</tr>
<tr>
<td>24-35</td>
<td>66</td>
</tr>
<tr>
<td>36-47</td>
<td>45</td>
</tr>
<tr>
<td>48+</td>
<td>56</td>
</tr>
</tbody>
</table>

Source: Mojarro and Aznar (1986, Table 8.4).
that this group contains a disproportionate share of premature infants, and the risk is merely due to prematurity rather than to the length of the interval. (On the other hand, as pointed out below, the short interval may itself be a cause of prematurity.) The excess mortality of those born before a short interval may be due to inadequate feeding and increased exposure to pathogens at vulnerable ages. But to estimate the importance of such effects analysts must first allow for reverse causation: the death of the first child may itself cause the subsequent interval to be short, either through a biologic effect (abrupt end of lactation leading to short postpartum amenorrhea) or a behavioral effect (grieving parents trying to quickly replace the lost child). As is true for the associations of maternal age and parity with infant mortality, the association of short interbirth intervals with infant mortality may be due in part to confounding variables, social characteristics of families that affect both the interbirth intervals and the risk of mortality independently. A likely suspect for such a confounding variable is access to health care. What has been found in rural Mexico is likely to be true of many other countries: women who use modern contraceptives tend to be the same ones who obtain good preventive and curative medical care for their children (Potter et al., 1987). Especially in the early stages of a national family planning program, the women using modern contraceptives are generally those with the most access to resources needed to promote the health of their children (Potter, 1988).

Even when relationships are easy to sort out conceptually, they can be difficult to sort out empirically. Data sets from high-mortality settings, especially retrospective data, contain many errors of dating.

One example of the possible effects of nonsampling error on the estimations of the associations discussed in this paper is differential accuracy of reporting dates in retrospective data. If the birth dates of children who subsequently died are more likely to be misreported than are the birth dates of children still alive at the time of the survey, then a higher proportion of both unusually short and unusually long intervals would either begin or end with the birth of a child who later died, even if there were no true bivariate association (directly causal or due to socioeconomic confounding variables) between interval length and mortality risk. Children who died are more likely to be omitted altogether in pregnancy histories, so it

---

13However, use of modern contraceptives and short interpregnancy intervals are not the same concepts. They may even be negatively associated. Bongaarts (1987) found in a cross-national comparison that average interbirth intervals (though not total fertility rates) tend to be lower in countries with higher rates of usage of modern contraceptives. In an analysis of micro-level retrospective data from Malaysia, DaVanzo and Starbird (1989) showed that the effects of a strong increase in contraceptive use (which would have led to longer intervals if other things had remained equal) were almost entirely negated by the effects of a strong decline in breastfeeding. Length of breastfeeding is associated with the length of the infecund period after birth and thus, on a population level, with the length of the interpregnancy interval. Average interbirth intervals changed little in Malaysia at a time when the total fertility rates were declining steadily.
is natural to expect that the reported birth dates of deceased children are more likely to be inaccurate than those of children still alive. Given the magnitude and ubiquity of the association between short intervals and infant mortality from studies with various designs, it is unlikely that such reporting artifacts account for much of the observed association, however.

**Effects on Length of Gestation and Birthweight**

The association of short interbirth intervals with higher risk of infant mortality appears to be mediated, at least in part, by low birthweight and premature delivery. The evidence linking short intervals with birthweight and prematurity comes from both rich and poor countries.

It is sometimes suggested that the relationship between short interbirth intervals and high rates of infant mortality is artifactual, a result of the fact that short intervals contain a disproportionate number of premature births. Unless short intervals caused the premature deliveries, reducing the number of short intervals would do nothing to lower infant mortality rates. But this view is contradicted by evidence that short intervals are associated with low birthweight and higher risk of infant mortality even when gestational age is held constant. Pebley and Stup (1987), for example, used prospective data from Guatemalan villages that contained information on gestational age to show that the association of short intervals from pregnancy outcome to next conception with infant mortality was similar to the association of short intervals between births with infant mortality. (Their procedure corrected, in other words, for any artifactual association by subtracting gestational age from the interbirth interval.)

Another study that defined intervals as the time between the preceding pregnancy outcome and the conception of the index child concerned a generally poor population belonging to a health maintenance organization in the East Bay area of northern California (van den Berg and Occhisi, 1984). Not controlling for maternal age, parity, or other variables, they found that 9.2 percent of conceptions less than 4 months after the previous outcome resulted in a pregnancy that terminated in less than 37 weeks. Where the interpregnancy interval was 4 to 7 months, the percentage fell to 6.8, and for intervals of 8 or more months it was 5.8 percent.

Placek (1977) analyzed data from the 1972 National Natality Survey in the United States in a way that allows separation of the association of interval length with gestational age from its association with birthweight (Tables 12 and 13). The National Natality Survey collected information for 1 in every 500 live births; only data for singletons born in hospitals to married women were presented. Table 13

14 Haaga (1986) presented evidence that in the Malaysia Family Life Survey the birth dates of children who later died were reported less accurately than those of children who lived.
TABLE 12 Percentage of Infants Weighing Less Than 2,500 Grams at Birth, by Preceding Birth Interval and Gestational Age, United States, 1972

<table>
<thead>
<tr>
<th>Interval Between Preceding Birth and Index Birth</th>
<th>Gestational Age</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 36 weeks</td>
<td>37-39 weeks</td>
<td>40+ weeks</td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>&lt; 12 months</td>
<td>43</td>
<td>4</td>
<td>3</td>
<td>8.8</td>
<td></td>
</tr>
<tr>
<td>13-24 months</td>
<td>27</td>
<td>8</td>
<td>3</td>
<td>7.5</td>
<td></td>
</tr>
<tr>
<td>25+ months</td>
<td>29</td>
<td>5</td>
<td>3</td>
<td>6.0</td>
<td></td>
</tr>
</tbody>
</table>

Source: Adapted from Placek (1977).

TABLE 13 Percentage of Infants by Gestational Age and Preceding Birth Interval, United States, 1972

<table>
<thead>
<tr>
<th>Interval Between Preceding Birth and Index Birth</th>
<th>Gestational Age</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 36 weeks</td>
<td>37-39 weeks</td>
<td>40+ weeks</td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>&lt; 12 months</td>
<td>13</td>
<td>38</td>
<td>49</td>
<td>100% (n = 213)</td>
<td></td>
</tr>
<tr>
<td>13-24 months</td>
<td>10</td>
<td>38</td>
<td>52</td>
<td>100% (n = 503)</td>
<td></td>
</tr>
<tr>
<td>25+ months</td>
<td>8</td>
<td>41</td>
<td>51</td>
<td>100% (n = 1,047)</td>
<td></td>
</tr>
</tbody>
</table>

Source: Adapted from Placek (1977).

shows that births after a short interval are more likely to be premature. This association could be causal, for example, if reproductive tissues have insufficient time to recuperate after one delivery. Also, a short interval could lead to cervical incompetence, which could lead to premature delivery. Table 12 shows that even within gestational-age categories infants born after a short preceding interval weigh less.15

In an analysis of prospective data from the Narangwal experiment in the Punjab, Fleming and Gray (1988) found an association between short preceding

15Judith Fortney (personal communication) has pointed out a source of potential bias affecting studies of this association, namely, doctors’ (or mothers’) revision of their estimates of gestational age after the birthweight is known.
intervals between pregnancy outcomes and low birthweight only for boys, not for girls. The reason for a sex differential is not apparent.

**Maternal Nutrition and Fetal Growth**

Maternal undernutrition is a commonly cited, almost a common-sense, explanation for the deleterious effects of a rapid succession of pregnancies. Women who live in communities where undernutrition (often seasonal) is common are known to put down much lower fat stores during pregnancy than women in rich countries or even to lose body fat during the course of a pregnancy; they also have smaller infants (NRC, 1970; Lawrence et al., 1987). Presumably it takes time after one pregnancy to rebuild stores, and the fetus of a closely following pregnancy could suffer if the mother is starting from a lower base. The energy cost of lactation is greater than that of pregnancy, so one would expect that the provision of nutrients to the first child of a closely spaced pair directly competes with the provision of nutrients to the second fetus (NRC, 1981).

Few of these causal pathways have actually been traced in human supplementation trials, and there is a good deal of disagreement in the interpretation of results from human supplementation trials and animal experiments concerning the ways in which fetal growth is constrained below genetic potential. Briand (1985) has summarized the results of supplementation trials in Guatemala, Senegal, and New York City: the energy cost of a “normal” pregnancy is about 40,000 calories, to produce a 3,500-gram baby. An additional 10,000 calories adds, on average, 30 grams to the weight of the baby (and even this is hard to document, since there are problems in the human trials of discounting all reverse causation, namely, that the women who were having bigger babies had bigger appetites). Perhaps the harshest environment for human supplementation trials to date was in rural Gambia, and there supplementation produced virtually no effect on birthweights during the dry season, but a large (approximately 220-gram) average effect for babies born during and just after the wet season. This difference was about the same as the pretrial difference in average birthweights between the two seasons. The Gambian results would have to be considered the upper limit of the size of an effect to be observed from maternal supplementation.

Some of the energy provided through supplementation is lost through (1) changes in the mother’s metabolism during pregnancy (supplementation increases the energy requirement of resting metabolism during pregnancy); (2) increased body fat deposition during pregnancy (the supplemented pregnant women in Gambia gained an average of about 2 kilograms of body fat over the course of their pregnancies, compared with about 3.8 kilograms typical in rich countries and no fat gain among the unsupplemented controls); and (3) increased activity for lactating women (the husbands of the Gambian women reported increased work output by the wives who received supplementation while lactating, even though the effects on milk output were quite small). These observations suggest
that the fetus and the nursing mother should be fairly efficiently protected against shortages in maternal energy intake. "It is only at very low levels [of prepregnancy weight and maternal weight gain] that the mechanisms for assuring the efficient conversion of maternal tissue into nutrients available for fetal growth are demonstrably compromised" (Kessel et al., 1985, p. 120). Winick (1983) speaks of the paradox that even undernourished women have enough nutrients in circulation to cover the apparent needs of pregnancy.

If anyone is suffering from an absolute energy shortage, it should be the mother. Yet other studies (summarized by Briand, 1985), even in West Africa, appear to show women maintaining fairly constant nonpregnant body weight through the course of multiple pregnancies. There are clinical descriptions of "maternal depletion syndrome" among poor women who have had many children, but simple anthropometry does not necessarily measure it.

Ferraz et al. (1988) analyzed data from a case-control study of singleton births in institutions in a small city in northeast Brazil. They found infants conceived after a short interpregnancy interval (6 months or less) to be at higher risk of IUGR, though not preterm delivery, than those conceived after longer intervals. The relative risk of IUGR was 1.38 for the infants born after a short interval, controlling for maternal age, education, smoking, and previous fetal loss or low birthweight. The relative risk was lowered somewhat, and lost statistical significance, when maternal prepregnancy weight was also controlled, which suggests that IUGR was caused by the maternal malnutrition associated with too short a recuperative period after the preceding pregnancy. Their ability to control for prior loss is especially helpful in distinguishing this hypothesized causal mechanism from simple recurrence risk.

Winick (1983) has suggested that the critical constraint is the ability of the placenta to transfer nutrients (rather than the availability of nutrients to the mother over the course of the pregnancy). Winick and Rosso have shown with animal studies that restricted energy intakes before and early in pregnancy lead to diminutions in the number of cells in the placenta and in cell size, which are associated with persistent neurological damage in baby rats. By contrast, starving the placenta later in pregnancy leads to smaller cell size but the same number of cells, with growth restriction but no persistent damage in the baby rats. Humans born with IUGR (but not major congenital anomalies) have placentas that weigh less than infants with appropriate weight for gestational age, due to a lower number of cells (Winick, 1967). Rosso et al. (1976) interpreted Winick's findings and the results of animal studies to mean that placental "capacity and efficiency" are affected by undernutrition at a crucial time in the first trimester of pregnancy.

A recent reviewer (Fox, 1986) doubts the evidence for gross structural problems with placentas; he and other critics of the "Winick school" adduce some evidence that the smaller fetus causes the smaller placenta rather than the other way around. Fox focuses instead on the "restricted supply of maternal oxygen
and nutrients as a result of inadequate transformation of the spiral arteries into uteroplacental vessels... a failure of the relationship between fetal and maternal tissues at a relatively early stage of pregnancy” (p. 517).

Both lines of explanation focus attention on early pregnancy and on the materno-fetal circulatory system rather than late pregnancy (when fetal growth is most rapid) and on the gross caloric intakes and the energy costs of lactation and pregnancy. For our purposes this makes more reasonable a relationship between adolescent pregnancy and rapid succession of pregnancies and fetal growth retardation. Even if it seems that there are enough nutrients to go around, placental function might be impaired if at the crucial stage of early pregnancy the mother is busy with recovery from a previous pregnancy, linear growth, and/or lactation.

Postpartum Nutrition

The postpartum nutritional status of infants born after closely spaced pregnancies would be affected if they were in competition for very limited family food supplies. Information on distribution of food intakes in families in poor countries is very hard to gather on a significant scale. A recent review (Haaga and Mason, 1987) concluded that there is fairly good evidence of discrimination against young girls in some parts of the world, especially South Asia, but there is little evidence of any tendency to discriminate against young children in general. Competition without discrimination would presumably operate to the disadvantage of both infants in a closely spaced pair. The older infant of such a pair has usually been considered the more vulnerable, since the arrival of the second infant can cause abrupt weaning. (Nutritionists always cite the example of the name kwashiorkor recorded by Cicely Williams in West Africa for a syndrome associated with protein deficiency, which apparently connotes the disease of the child who has been displaced.)

The problem of untangling reverse causation is difficult in demographic studies. Early weaning can itself shorten the birth interval in the absence of efficient contraception. However, Millman and Cooksey (1987) found that little of the association between short birth intervals and increased risk of infant mortality for the second infant of the pair could be accounted for by the addition of information on breastfeeding. Fleming and Gray (1988) also point out that the effects of a short succeeding interval can be spurious, confounded by the effects of a short preceding interval with which the succeeding interval is associated.

In data from the Machakos district of eastern Kenya there was a fairly constant effect (300 grams at 2 months, not statistically significant) of short preceding birth intervals on children’s weight, persisting to age 36 months, but there was no consistent effect of a short succeeding interval (Boerma and van Wieren, 1984). This would tend to support the hypothesis of an effect on fetal growth rather than postpartum nutrition.
Infectious Diseases

Infectious diseases—primarily neonatal tetanus, diarrheal diseases, and respiratory infections (pneumonia and influenza)—account for the majority of infant deaths in high-mortality countries (Chen, 1983). It is not necessary, but certainly likely, that many of the excess infant deaths associated with extremes of maternal age or parity and with short birth intervals have infections as a proximate cause. There are two (not mutually exclusive) ways in which a risk factor can increase the probability of death from an infectious disease: by increasing exposure to pathogens or by lowering the resistance of the host to infection.\(^{16}\) Infections could affect the fetus directly (either traveling across the placenta or, after the membranes have ruptured, through direct contact in the process of birth) or indirectly (if a maternal infection causes premature rupture of the membranes or premature delivery or retards fetal growth.) Low weight for age, both at birth and postnatally, is associated with depressed immunocompetence (Suskind and Partington, 1981) and with greater risk of death due to infectious diseases, especially respiratory infections (Kielmann et al., 1983; Barros et al., 1987a, 1987b).

How could infections differentially affect children born at different parities, or to women of different ages, or after short birth intervals? Exposure for the fetus would be associated with biodemographic factors: (1) if young mothers or mothers who already have a young baby (short interval) or many children in the house (high parity) are more likely to get infectious diseases during pregnancy that are known to affect the fetus or (2) if premature rupture of the membranes, more common among older women (and high-parity women?), puts a baby at greater risk of intrapartum infection. Postnatal exposure of the infant would be associated with biodemographic variables if (3) the presence of a young sibling (short interval) or a large number of siblings (high parity and/or short interval) increased contacts with pathogens. Postnatal susceptibility might be increased if (4) the infant at risk by one of the biodemographic criteria is more likely to be premature or undernourished at birth (IUGR) or subsequent to birth. The first three potential pathways are discussed below. The fourth was discussed earlier.

Maternal Infections

A fetus is better protected from infections than she or he will ever be after birth. But there are maternal infections (mostly viral) that can affect the fetus. Overall (1987) presents a useful summary of the evidence on the effects of maternal viral infections on the fetus and neonate. The four most important

---

\(^{16}\) Many infectious agents are just about ubiquitous and everyone has some contact with them, but symptomatic infection (e.g., diarrheal diseases) is more likely the larger the number of pathogens that invade or the more frequent the contact with them. So “exposure” for many diseases should be thought of as “likelihood of sufficiently heavy or frequent contact.”
infectious agents are cytomegalovirus (CMV), rubella, hepatitis B, and herpes simplex. Except for rubella, which is transmitted only to the fetus, each can result in a congenital, intrapartum, or postnatal infection in the infant. CMV and herpes simplex virus have been associated with many negative outcomes for the fetus/neonate: fetal death, prematurity, IUGR, malformations, congenital infection, acute postnatal infection, and persistent postnatal infection. Rubella is associated with all these except acute postnatal infection. Hepatitis B (which is endemic in many developing countries, e.g., in Southeast Asia) also has been linked to prematurity and fetal and neonatal infectious disease (Overall, 1987).

Nonviral maternal infections are less likely to cross the placenta, but they may still affect the fetus before or during labor, especially if the membranes have ruptured prematurely.

Premature rupture of the membranes (PROM) and preterm labor in general pose a severe risk of infant mortality. Infants born after PROM are at increased risk of neonatal infections, perinatal asphyxia, and respiratory distress syndrome [though for the latter the risk associated with PROM is less than that associated with other types of premature labor (Blackmon et al., 1986)]. "Neither the etiology of premature rupture of the membranes nor of premature labor is known. However, a growing volume of experimental and clinical data strongly supports genital infection either directly or indirectly as a major cause of both" (Alger and Pupkin, 1986:760). Genital infections are more common among poor and uneducated women than among those with better access to health care and those who practice better hygiene. To the extent that the high-risk groups defined by the bioclimatic variables include more poor women, they can be expected to experience premature labor more often, with negative consequences for the neonate.

Maternal parasitemias—fungal or bacterial infections that can affect the fetus—include toxoplasmosis, syphilis, tuberculosis, and trypanosomiasis. In general, congenital infections may produce symptoms at birth, but in the majority of cases they are insidious, producing symptoms after some months (Berkowitz, 1984). Presumably even a congenital infection that is not itself a leading direct cause of infant deaths may render the infant more susceptible to later infection.

Ascending infections to which a baby is vulnerable after the membranes have broken include septicemia and pneumonia. During a baby's passage through the birth canal, she or he is susceptible to infections of the mother's urinary tract, including CMV and fecal bacteria (Berkowitz, 1984).

Most of these infections are prevalent in developing countries. CMV is very widespread in both rich and poor countries; one source estimates that the prevalence of CMV seropositivity in women ranges from 8 percent to 60 percent worldwide (Peckham et al., 1987). CMV has been called "a significant pathogen

\[17\] Malaria is discussed separately above.
of the human fetus capable of producing disease ranging from subtle abnormalities not detectable at birth to severe multisystem disease" (Wright, 1980, p. 170). On the other hand, "the fate of infants born with asymptomatic CMV is not clear" (Wright, 1980, p. 170). Rubella is highly communicable and has been shown to cause severe fetal abnormalities. Urinary tract infections, very common in poor countries and among poor people in rich countries, are associated with a sharply increased likelihood of low birthweight (due to prematurity, IUGR, or both?). Sever et al. (1977) matched pregnancies in the Collaborative Perinatal Survey in the United States by maternal age, race, birth institution, and socioeconomic status and found a relative risk of 3.7 for stillbirths to women with urinary tract infections; 1.5 for a birthweight of 2,000 to 2,499 grams; 2.8 for a birthweight of 1,500 to 1,999 grams; and 4.5 for a birthweight below 1,500 grams. Gazaway and Mullus (1986) reported a relative risk of preterm labor of 3.8 in pregnant women with bacterial vaginosis compared with those without it.

What is missing for almost all of these congenital infections is strong evidence that maternal exposure or susceptibility is related to biodemographic variables. Older mothers (and grand multiparae?) are known to suffer a greater incidence of PROM, which may increase the risk of intrapartum infections. There is evidence that malaria in particular affects the growth of the fetus and the transmission of maternal immunoglobulin at parity 1 (see above).

Of the other infectious agents, CMV is a good candidate for more research. There are recent studies from Britain and the United States that show the ease with which it can be passed in either direction by a nursing mother and an infant, and older siblings may bring CMV home from day care settings and infect their pregnant mothers (Peckham et al., 1987).

Increased Postnatal Exposure to Pathogens

The two most common routes for postnatal infections are fecal-oral and respiratory-respiratory (Chen, 1983; Stanfield, 1987). A child born at high parity is likely to live with many siblings, and if the births have been closely spaced, these will be young siblings. A child born within a year after the previous child will reach the age at which immunities acquired across the placenta or

\footnote{The most common deadly disease transmitted otherwise than these two routes is neonatal tetanus, usually caused by septic cutting and sealing of the umbilical cord. Stanfield and Galazka (1984) summarized community surveys of causes of infant deaths, mostly from South Asia and Sub-Saharan Africa, showing that about 20 to 40 percent of neonatal deaths in these high-mortality regions are caused by tetanus. I found no literature showing any relationship between tetanus infection and the biodemographic variables of interest. Ronald Gray (personal communication) has suggested that there may be a link due to a lower likelihood of some pregnant women (e.g., young women, primiparous) receiving antenatal tetanus immunization. If so, this would represent another case in which the biodemographic variables are markers for social factors affecting maternal and child health, rather than causal factors.}
through breast milk (3 to 9 months) when the next older sibling has become mobile and is likely to be in contact with all sorts of pathogens (15 to 21 months). Some studies of measles mortality in rural and periurban Guinea-Bissau have showed that crowding, specifically the number of other children in a household, is a better predictor of measles mortality than are anthropometric indicators of nutritional status (Aaby et al., 1983; Smedman et al., 1987). Though they do not report causes of death by birth order, the authors of the summary report on the Narangwal experiment in maternal and child health services in the Punjab report excess mortality among children above birth order seven (twice the rate for the whole sample), with most deaths in the sample caused by gastrointestinal and respiratory infections (Kielmann and associates, 1983).

Infections transmitted via feces are very important as causes of infant deaths and may be facilitated by the presence of many children, especially young ones, in the household. A recent study showed that 55 percent of cholera cases in Bangladeshi villages could be attributed to the excess risk posed by having an asymptomatic breastfeeding child who has cholera vibrio in her or his stools (Riley et al., 1987). Riley et al. surmise that careless handling of an infant’s feces facilitates transmission. This would be a specific reason for young siblings, rather than just many siblings, being a risk factor, which would account for an association of close birth spacing with infant health. Similarly, another study from the International Center for Diarrheal Disease Research in Bangladesh (apparently of different villages) found infant mortality to be higher in households with more than 10 members than in smaller households—a relative risk of 1.5 in an analysis controlling for several other economic and demographic variables (Rahman et al., 1985). In this sample, the authors argue, such large households tend to have more than two adult earners and thus are not poorer than smaller households, thus reversing one effect that confounds crude household-size mortality differentials in other samples. Diarrheal diseases were the leading cause of infant morbidity and mortality in this sample, and the authors suggest that careless handling of the feces of small children explains the significant effect of household size. Yet another analysis from the same institution showed specifically that the presence of other children in the household who are less than 5 years old was associated with worse nutritional status as measured by anthropometry for boys (though apparently not for girls), even when measures of social and economic status were controlled (Becker et al., 1986). This finding is compatible with any of the three effects discussed here—prenatal nutrition, postnatal nutrition, and infectious disease.

Conclusions

Of the biodemographic risk factors discussed here, the state of knowledge about intermediate mechanisms for short interpregnancy intervals is the least satisfactory. This is especially unfortunate because the direct impact of family
planning programs on infant health (apart from their association with prevention of unwanted births and better provision of maternal and child health services) is expected to come about largely from a decrease in the number of exceptionally short intervals.

In my view the best evidence is for some mechanism interfering with the development in early pregnancy of the uteroplacental circulatory system, leading to fetal growth retardation. There may also be problems with reproductive tissues (e.g., cervical incompetence, which leads to premature delivery). This latter mechanism could, at the same time, be a sort of statistical artifact (short intervals just happen to include more of the infants born, for unrelated reasons, after short gestation) and a true causal chain—inadequate recuperation from the first parturition, leaving structures too weak to support the next pregnancy. The WFS studies have found short intervals to be associated with an excess risk that continued well past early infancy, but this is consistent with both prematurity and fetal growth retardation as causal mechanisms, since infants born too small and too early who survive the neonatal period may still have respiratory and immunologic problems that weaken them later.

A high priority for further research should be the collection of information on birthweights, gestational ages, and causes of death in association with data on pregnancy intervals (preferably entire reproductive histories). This includes many variables that are extremely difficult to collect in field studies, of course, but the selectivity of hospital samples may be too great in populations where the attributable mortality risk is high enough. Where demographic surveillance systems are in place, a useful study design might be a case control, matching each short-interval death with a normal-interval death and comparing proximate causes, ages at death, and risk factors.

It would be interesting to isolate the effect on infant health of a "pure" reduction in the proportion of short interpregnancy intervals, unaccompanied by changes in women’s education, their social roles, access to other health services, etc. Insofar as family planning programs actually do bring about a reduction in the proportion of short intervals, measuring this effect would allow us to estimate the benefits in terms of child health of increased effort in family planning programs. (We are leaving aside the effect of family planning programs on the number of dependents in each child’s family and thus the number of competitors for presumably limited health-related resources.)

The very success of a family planning program in a new geographic area or in a poorer social class provides evidence that women’s roles and their ability and willingness to use health-related resources and knowledge, among other things, have changed and are changing. To some extent the effects of confounding and unobserved variables on estimating the effect of interval length on infant mortality can be alleviated by better measurement of social, economic, and other health-related variables and by careful specification of statistical models. Such research
will help policymakers assess the most effective mix of components of health services (including family planning) in different settings.

ACKNOWLEDGMENT

I received very helpful advice, comments, and references from many members of the working group and from others who reviewed earlier drafts of this paper. In particular, I would like to thank Julie DaVanzo, Peter Donaldson, Judith Fortney, Ronald Gray, Jorge Martinez-Manatou, Anne Pebley, Joseph Potter, and James Trussell for all of their assistance.

REFERENCES

Aaby, P., J. Bulsh, I. M. Lisse, and A. J. Smets

Alberman, L.

Alger, L. S., and M. J. Popkin

Allen, G.

Anderson, G. D., and B. Sahai

Bakketeg, L. S., and H. J. Hoffman

Barros, F. C., C. G. Victora, J. P. Vaughan, A. M. B. Teixeira, and A. Ashworth

Barros, F. C., C. G. Victora, J. P. Vaughan, and H. J. Estanislau

Becker, S., R. E. Black, K. H. Brown, and S. Nahar

Berkowitz, L. D.

Blackmon, L., L. S. Alger, and C. Crenshaw


Fortney, J. A., and J. E. Higgins  


Fox, H.  

Gazaway, P., and C. L. Mullis  

Geronimus, A. T.  

Haaga, J. G.  

Haaga, J. G., and J. B. Mason  

Haas, J. D., H. Balsazare, and L. Calfield  


Hansen, J. P.  

Harrison, K. A.  

Holley, W. L., A. L. Rosenbaum, and J. A. Churchill  

Hook, E. B.  

Hull, T., and B. Gubhaju  

Institute of Medicine (IOM), Committee to Study the Prevention of Low Birthweight  
Kane, S. H.
Kessel, E. S., Saxtriawata, and S. D. Mumford
319(Suppl.):120–127.
Kielmann, A., and associates
1983 Child and maternal health services in rural India: the Narangwal experiment.
University Press.
Kiely, J. L., N. Pameth, and M. Susser
1986 An assessment of the effects of maternal age and parity in different components of
Klebanoff, M. A.
1988 Short interpregnancy interval and the risk of low birthweight. American Journal of
Kramer, M. S.
Lawrence, M., W. A. Coward, F. Lawrence, T. Cole, and R. Whitehead
1987 Fat gain during pregnancy in rural African women: the effect of season and dietary
Lawson, J. B., and D. B. Stewart
1967 Obstetrics and Gynecology in the Tropics and Developing Countries. London:
Edward Arnold.
McAnarney, E. R.
1987 Young maternal age and adverse neonatal outcome. American Journal of Diseases in
Childhood 141:1053–1059.
McGregor, I. A.
1984 Epidemiology, malaria, and pregnancy. American Journal of Tropical Medicine and
Hygiene 33:517–525.
Mehta, L., and I. D. Young
1987 Recurrence risks for common complications of pregnancy. Obstetrical and
Gynaecological Survey 42:218–223.
Millman, S. R., and E. C. Cooksey
1987 Birth weight and the effects of birth spacing and breastfeeding on infant mortality.
Mojarro, O., and R. Aznar
1986 Influencia de los factores biologicos y del estructura social en la mortalidad infantil,
y Salud en el Mexico Rural. Mexico City: Instituto Mexicano del Seguro Social.
Naeye, R. L.
1981 Teenaged and pre-teenaged pregnancies: consequences of the fetal-maternal
1983 Maternal age, obstetric complications, and the outcome of pregnancy. Obstetrics and
Naeye, R. L., N. Tafiri, C. C. Marhoe, and D. M. Judge
National Research Council, Committee on Maternal Nutrition
Academy of Sciences.
National Research Council, Committee on Nutrition of the Mother and the Preschool Child
Niswander, K. R.
Stanley, eds., The Epidemiology of Prematurity. Baltimore, Md.: Urban and
Schwarzenburg.
Niswander, K. R., and M. Gordon
1972 The Women and Their Pregnancies: The Collaborative Perinatal Study of the
National Institute of Neurological Diseases and Stroke. Philadelphia: W. B.
Saunders.
Ojo, A., and V. Oromoye
Overall, J. C.
Cherry, eds., Textbook of Pediatric Infectious Diseases, 2nd ed. Philadelphia: W. B.
Saunders.
Pebbley, A. R., and P. W. Stupp
1987 Reproductive patterns and child survival. International Family Planning Perspec-
tives 12(3):71–79.
Peckham, C. S., C. Johnson, A. Ades, K. Pearl, and K. S. Chin
1987 Early acquisition of cytomegalovirus infection. Archives of Disease in Childhood
Placek, P.
1977 Maternal and infant health factors associated with low infant birth weight: findings
Stanley, eds., The Epidemiology of Prematurity. Baltimore, Md.: Urban and
Schwarzenburg.
Potter, J. E.
1988 Birth spacing and child survival: a cautionary note regarding the evidence from the
Potter, J. E., O. Mojarro, and L. Nunez
1987 The influence of health care on contraceptive acceptance in rural Mexico. Studies in
Family Planning 18:144–156.
Powell-Griner, E.
1987 Risk of Perinatal Death: A Log-Linear Analysis of the Effects of Selected Factors on
Pregnancy Outcome. Paper presented to the annual meeting of the Population
Association of America, Chicago Ill., May.
Preston, S. H.
Hobcraft, eds., Reproductive Change in Developing Countries: Insights from the
Puffer, R. R., and C. V. Serrano
1973 Patterns of Mortality in Childhood. PAHO Scientific Publication No. 262.
1975 Birthweight, Maternal Age, and Birth Order: Three Important Determinants in Infant
Health Organization.
Rahman, M., B. Wojcinski, and K. M. S. Aziz
1985 Impact of environmental sanitation and crowding on infant mortality in rural
Riley, L. W., S. H. Waterman, A. S. G. Fanque, and M. I. Huq

Rosso, P., M. Wasserman, S. J. Rozowski, and E. Velasco

Royston, E.

Santow, G., and M. D. Bracher

Seeds, J. W.

Seidman, D. S., R. Gale, P. E. Slater, P. Even-Hadani, and S. Harlap

Sever, J. L., J. H. Ellenberg, and D. Edmonds

Smedman, L., G. Sterky, L. Mellander, and S. Wall

Stanfield, J. P., and A. Galazka

Stanfield, S. K.

Strobino, D. M.

Suskind, R. M., and M. Parington

Swanson, C. A., and J. C. King

Tsu, V. D., and N. Newton

van den Berg, B. J., and F. W. Oechsl

Villar, J., and J. M. Belizan
WHO Malaria Action Programme
Winick, M.
World Health Organization
World Health Organization, Family Health Division
Wright, H. T.