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The risks of having children in later life

Social advantage may make up for biological disadvantage

General practice
p 1708

When is the best time in life to be a mother? Or a father? These questions have been raised in the past, but the answers have left uncertainties. To address some of these issues, Andersen et al, in their paper on maternal age and fetal loss in this issue of the *BMJ,* have used a large set of data from the Danish Epidemiology Science Centre to good effect (p 1708).[1] Their findings are largely confirmatory: older age strongly increases a woman's chances of at least three untoward outcomes—namely, stillbirth, miscarriage, and ectopic pregnancy. Prospective parents concerned about their age might hope for answers to other questions as well.

Over the past 50 years or so, options for controlling or enhancing fertility have grown. These changes began with the introduction of oral contraception and have continued with the legalisation of induced abortion and the development of ever more sophisticated techniques of in vitro fertilisation and advances in obstetrics that ensure safe deliveries. Older women especially benefit from all of these; each has had an impact on the age at which women bear children.

For instance, the Danish tables show trends in the rates of induced abortions over the period 1978-92. On one side of the reproductive age span, these occur proportionately most frequently during the teens, when the greatest social disadvantage is associated with childbearing. On the other side, the greatest number of induced abortions occur at the latest ages, when the greatest biological disadvantage is associated with childbearing.

The collection of such large bodies of data limits the social and biological variables that can be recorded. Still, the data reported by Andersen et al might have been stretched further. For example, they provide a mean length of gestation for miscarriages rather than a distribution over the range of specific gestational ages. Such an analysis obscures the relation between miscarriages at different stages of gestation and maternal age.[2] The greatest concentration of chromosomal anomalies and by far the highest rate of pregnancy loss is found early in gestation. At least 90% of such losses occur during the first trimester. At the same time, those anomalies that are trisomic and those fetuses that are most viable are strongly related to maternal age.

Also, it may not be asking too much of routine data on stillbirths to differentiate between antepartum and intrapartum losses. In recent years in developed countries most losses occur before labour, and only in these is an effect of maternal age observed.[3] Hypotheses about the causes of antepartum stillbirths occurring at advanced maternal age have included chromosomal anomalies, pre-eclampsia (especially in nulliparous women), and diabetes. None of these factors, however, contributed to the age effect observed in a large data set on stillbirths in Canada collected from 1961 to 1993.[4] Unlike the Danish series, in this perspective over a longer time, data did show a considerable decline in the overall rate of stillbirths. It is also notable that older mothers shared in this general long term decline. Thus, among women aged 35 years or older, the rate of stillbirths per 1000 births decreased from 16.5 in 1960-9 to 5.8 in 1990-3. Though the higher relative risk for older women persists, their absolute risk has been greatly reduced.

Maternal age has an impact on other aspects of reproduction for which information might not have been available in the Danish register. Among those that are usually recorded are multiple births and congenital malformations. Delayed conception or infertility, although certainly of interest, will often not be recorded.

The incidence of multiple births increases with the age of the mother but distinctly more so for dizygous rather than for monozygous twins and more so still for triplets.[5] In recent times, however, infertility treatment has increased the rate of all multiple births, and this surely confounds the effects of natural age.

When birth defects are considered, older women have a consistently increased risk only for Down's syndrome, which is less of a hazard now than it was, owing to the advent of prenatal screening. Not as well known is the fact that certain rare disorders, such as achondroplasia, are more common among births to older fathers.[6] Some of these, presumed to be new mutations, are detectable in offspring only later in life; schizophrenia is one example.[7 8]

Information on parental age and infertility, which is usually beyond the scope of routine records, is important in advising prospective parents. Thus, Andersen et al, like other authors, provide estimates of fetal loss occurring between the time a pregnancy is recognised and a live birth.[1] But, in addition to fetal loss, older couples are more likely to have subfertility or infecundability (failure to conceive). If a recognised pregnancy occurs, the simple recording of the "time to conceive" yields a relative measure of fecundability. Beyond the scope of routine records, studies that have used highly sensitive human chorionic gonadotrophin tests to look at very early pregnancy have helped to

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distinguish between an absolute failure to conceive and loss before the first missed period.[9] Older women do worse in both respects.[10] When oocytes are randomly assigned to women of various ages during in vitro fertilisation procedures (in which the uterus is hormonally prepared), embryos implant equally often among women older than 40 and among younger women. Still, older women are less successful in sustaining an embryo.[11] Outside the experimental situation, age carries the added risk of a trisomic oocyte. Thus, in real life the older woman carries two independent risks: firstly, of conceiving a trisomic oocyte, and, secondly, of having a less efficient uterus. Neither of these risks is an absolute bar to childbearing; successful pregnancies do occur, if seldom, up to age 45 or older.

Typically, menstruation and ovulation cease with the menopause, at around age 51 or 52. Yet women in their late 40s seldom conceive and complete a pregnancy without the assistance of modern techniques. Classic studies in populations that do not use contraception, such as the Hutterites, show that childbearing declines steeply well before that time as women pass into their 40s.[2]

The reasons for this decline in fertility as a woman ages relate to both the oocyte and the uterus. Although the oocyte becomes increasingly vulnerable with age, remarkable technical advances have substituted for failing physiological nurture of embryos. When embryo replacement was first achieved, women aged over 35 were seen as poor candidates for the procedure. Now, with better hormonal control, older women are often successfully treated.

Finally then, after potential parents have weighed the age factor in terms of conceiving and carrying a pregnancy to term, they might be comforted to know that a child born to older parents does have advantages. In some studies that have controlled for social factors and parity, such children do better at school than those of very young parents.[12 13] In the demanding task of raising children older parents may be less resilient than younger ones, but their experience and knowledge are almost bound to be greater, their economic situation better, and child rearing more affordable. Biological disadvantage is to a degree balanced by social advantage.

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The epidemiology of stomach cancer: correlating the past with the present

Socioeconomic influences in early life can influence mortality in adult life

Studies of geographical correlation have low status within the canons of evidence based medicine. At times, the low status is not without reason—most readers will be familiar with presentations in which the equivalent of the international variation in childbirth is attributed to the nesting patterns of storks. Every so often, however, a simple correlation synthesises a complex web of research hypotheses and findings and shows a striking relation not previously appreciated.

Leon and Davey-Smith present one such picture in this week's *BMJ* (p 1705). Their graph plots the mortality from stomach cancer in 1991-3 among 65-74 year old men against infant mortality in 1921-3 in 27 countries and shows a strong relation between the two. The strength of the correlation is nearly identical for mortality from stomach cancer in women and changes little when adjusted for current (1991-3) infant mortality in each country. In contrast, the correlation between deaths from stomach cancer and current infant mortality is weaker, approaching zero when adjusted for infant mortality in 1921-3.

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A parsimonious interpretation of these results is that among the 65-74 year olds who died in 1991-3 the two measures of infant mortality represent national indicators of socioeconomic development around the times of their births and deaths. Mortality from stomach cancer seems to be strongly associated with general socioeconomic conditions at the time of birth but not at the time of death. The pattern for mortality from tuberculosis is similar to that for stomach cancer, whereas mortality from stroke correlates strongly with both past and current measures of infant mortality.

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