

Periconception window: advising the pregnancy-planning couple

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Objective: To discuss the importance of the periconceptional window with regard to being a critical window of exposure. To review the empirical data related to healthy periconceptional behaviors.

Design: Literature review.

Conclusion(s): Human reproduction is a couple-dependent process. Recent literature has highlighted that the periconceptional time period is a critical window of exposure that can impact growth and development. In advising the pregnancy-planning couple, it is of paramount importance that couples have knowledge of the timing of the fertile window to ensure that intercourse occurs on days with the maximum probability of pregnancy. Many women adopt healthier lifestyles while trying to conceive, often quitting smoking, eating healthier or taking vitamins. However, there is a lack of empirical data from prospective studies regarding which environmental exposures or behaviors are or are not safe. Noticeably absent are data regarding the effect of male partners' exposures or behaviors on couple fecundity and fertility. As we improve our ability to pinpoint the timing of conception, we should be able to better advise couples planning pregnancy. (Fertil Steril® 2008;89:e119–21. ©2008 by American Society for Reproductive Medicine.)

Key Words: Critical windows, environment, parental exposures, preconception, pregnancy planning

Successful human reproduction and development requires completion of a series of highly interrelated and time-dependent processes involving both partners of the couple. Human reproduction is a relatively inefficient process in comparison to other species (1). This is evidenced by human reproduction's highly selective survival process that commences with the development of follicles and the eventual selection of a single dominant follicle for ovulation, followed by a relatively low probability of conception, implantation, and embryonic survival. Prospective pregnancy studies with preconception enrollment of women report cumulative probabilities of pregnancy at 1, 3, and 6 months of trying to conceive as ranging from 38%–43%, 60%–68%, and 81%–94%, respectively (2, 3).

The loss of conceptions among fecund couples, or those biologically capable of reproducing, supports the vulnerability of the human conceptus during the earliest stages of human development. As recently reviewed, the periconception window is one of the earliest critical windows for human development (4). The absence of a biomarker of human conception challenges investigators' ability to obtain

empirical evidence regarding the parental determinants of human fecundity and fertility. Studies focusing on couples undergoing assisted reproductive technologies, however, offer new insight about early parental influences on the developing human organism. For example, oocyte quality has been positively associated with embryonic quality (5, 6). Noticeably less research has focused on paternally mediated factors, although a positive association between sperm morphology and blastomere cleavage rate (7) has been reported, as have centrosome defects and disorders of fertilization or early development (8).

The purpose of this article is to briefly describe the critical windows of human development, assess the current research data available on parental determinants of human fecundity and fertility, and discuss the recommendations and guidelines available to the pregnancy-planning couple.

PERICONCEPTION CRITICAL WINDOW

A critical window may be defined as the time-sensitive interval during which exposures or events disrupt or interfere with the physiology of a cell, tissue, or organ (9). It is a period characterized by marked cellular proliferation and development and numerous changing metabolic capabilities in the developing organism (10). Dose-dependent exposures during this window may result in adverse permanent and irreversible effects. Investigators have suggested the need to define both critical and sensitive periods in recognition that exposures during the latter may still affect development or result in eventual adult disease, but with reduced magnitude in comparison to exposures within critical windows (11).

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We define the periconception window as the time preceding, including, and immediately following human conception. This definition allows for variability in operationalizing the lower and upper bound of the window depending upon the research question. This is particularly important given the increasing evidence that in utero exposures may have intergenerational effects (12). For example, intrauterine growth restriction is associated with poorer ovarian development, smaller ovaries, greater anovulatory cycles, and diminished responsiveness of the female to follicle stimulating hormone (13, 14). Among males, intrauterine disturbances in hormonal milieu have been associated with hypospadias, cryptorchidism, diminished sperm counts, and testicular cancer collectively described as the testicular dysgenesis syndrome (15). Men with testicular cancer are reported to have diminished fecundity before diagnosis, suggesting that impaired fecundity may be on the causal pathway to this cancer or another manifestation of the underlying defect (16). Thus, the periconception window offers researchers an ability to measure potential toxicants while assessing the epigenetic influences within the context of exogenous and endogenous factors (e.g., nutrition, environment, stress, and medications). Choice of the operational definition of the periconception window rests in part upon the study question and characteristics of the exposures and behaviors under study.

ADVISING THE PREGNANCY-PLANNING COUPLE

The absence of a biomarker for human conception limits our ability to develop a body of empirical and reproducible evidence that can be used to develop preconception guidelines. However, clearly, it is of paramount importance that couples understand how best to time intercourse to achieve pregnancy. Recent evidence underscores the need to time intercourse during the 6-day fertile window to maximize conception probability while considering parental ages (17–19). Investigators have found that many women do not know “their” true fertile window. In fact, only 25%–30% women have all the days of their fertile window fall between days 10 and 17 of their menstrual cycle, which is often cited as “the” fertile window (20, 21).

Women desirous of pregnancy actually adopt healthy behaviors such as reducing use of cigarettes and alcoholic beverages (22, 23) and increasing use of multivitamins including folic acid for the reduction of neural tube defects (24, 25) as recommended in clinical and public health messages. We are unaware of any research focusing on women or couples’ behavioral intentions while attempting pregnancy with regard to preconception guidance. This may reflect a limited number of prospective pregnancy studies with preconception enrollment of women assessing lifestyle and behavioral influences on human reproduction and development (26). The best evidence we have detailing the effect of parental exposures on the conceptus and early embryo comes from these studies. Most have focused on behaviors such as cigarette smoking, alcohol and caffeine consumption, intercourse patterns, and

extremes of body mass index among women trying to become pregnant.

We are unaware of articles employing quantitative methods for pooling and weighing the results of individual studies save for a few expert reviews (27, 28). Suffice it to say, smoking, alcohol, and caffeine consumption have been associated with diminished female fecundity as measured by a longer time to pregnancy (29–32), although often with equivocal results or of varying magnitude. In addition, at least one investigator has reported a negative relation between perceived stress (33) or douching practices (34) and female fecundity.

PRECONCEPTION CARE

A recent survey of the membership of the American College of Obstetricians and Gynecologists reported that physicians think preconception care (PCC) is important, and 95% recommend it to women planning pregnancies but only 54% to sexually active women (35); however, 49% of respondents reported that patients actually seek PCC. A systematic search of the literature from 1996–2005 regarding PCC concluded the absence of current comprehensive guidelines and the lack of formal evaluation of clinical guidelines (36). However, recently, the Centers for Disease Control and Prevention released PCC guidance that focuses on the importance of accessing health care for the pregnancy-planning couple (37).

Public health messages should recognize that some exposures are avoidable while others are not. Engaging in moderate physical activity and exercise is important for fecundity and general well being, as is enjoying a healthy diet, maintaining a healthy weight, avoiding exposure to active and passive cigarette smoke, and avoiding consumption of alcoholic and caffeinated beverages. Following guidelines for preparing fish meals (trimming the fat, removing or puncturing the skin, and choosing a method other than frying for cooking the fish) may also help to reduce exposure to persistent chemicals and metals. These are but a few of the many potential lifestyle or behavioral factors that may impact couple’s fecundity and/or fertility. Increasingly, investigators are recognizing the potential for long-term health implications associated with intrauterine exposures. As a result, interest is arising in a life course approach to the study of chronic diseases so that the many etiologic pathways operating over an individual’s life can be considered in the context of disease etiology (11). In sum, quantifying exposures during critical windows including the periconception window may identify direct effects on the developing organism over the course of his/her lifespan and, potentially, that of future generations. As new data emerge regarding effective strategies for avoiding environmental exposures to persistent or short-lived compounds, more specific advice should become available.

In summary, the absence of data on the effect of periconceptional parental exposures and human reproduction and development limits our ability to develop evidence-based

preconception guidelines that are responsive to the couple-dependent nature of human reproduction and development. Targeting messages tailored to both partners of the couple is an important step in developing public health campaigns promoting healthy behaviors during all critical windows of human development including the periconception interval. Ultimately, formal evaluation of such guidelines is needed along with their lasting impact on couples' behavior. Although researchers strive to fill critical data gaps about the effects of the environment as globally defined on human reproduction and development, the public may do well to continue behaviors such as healthy eating, engaging in moderate exercise, and consulting clinicians when in doubt to mitigate the effects of exogenous agents not under their control. Given the evolving body of evidence supporting considerable reprogramming of embryos and fetuses in relation to in utero stimuli, the importance of the periconception window in relation to parental environmental exposures and behaviors cannot be understated. To this end, purposeful research is not only timely but needed so that the advice we offer couples is empirically or evidenced based.

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