

Opinion paper

Optimization of women's health before conception when pregnancy has been postponed

Joachim W. Dudenhausen¹, Amos Grunebaum¹ and Ursula M. Staudinger²

¹ Department of Obstetrics and Gynecology, Weill Medical College of Cornell University, New York, NY, USA

² Jacobs Center of Lifelong Learning and Institutional Development, Jacobs University Bremen, Bremen, Germany

Abstract

Objectives: In the industrialized world, the mean age at which mothers give birth to their first child has increased. The purpose of this article was to review the available evidence in order to optimize preconception care in women who have postponed childbearing to the later years of the reproductive life cycle.

Methods: Review of literature.

Results: There is a paucity of evidence and rigorous studies to advise mothers on the potential interventions for optimizing pregnancy outcome.

Conclusions: Evidence-based guidelines for advising women who postponed childbearing are scant, and further research in this important area is urgently needed.

Keywords: Delayed motherhood; nutrition; plasticity; preconception care.

Introduction

Demographic statistics indicate that, over recent decades, there has been a considerable increase in the mean age at which mothers in the industrialized world give birth to their first child. For example, in Bavaria (Germany), since the 1980s the share of pregnant women accounted for by the age group 35–39 has roughly tripled from 4% to 12% [17]. In the United States, between 1990 and 2001 the rate of those giving birth in the age groups 35–39, 40–44, and 45–49 increased by 30%, 47%, and 190%, respectively [5]. This development toward later childbearing also needs to be seen in conjunction with the tremendous extension of the average life expectancy (i.e., by 45 years) that modern societies have experienced during the last 150 years.

Much emphasis has been placed on the relations between the frequency of chromosomal anomalies and advancing maternal age, as well as the risk of multiple pregnancies in women with late motherhood. However, the extensive literature on the risks of late motherhood both for the mother and the fetus, and on the subsequent prognosis for the child

rarely features in the public debate. The data in the literature on the medical risks of late motherhood are contradictory. It is striking that in societies with a high incidence of late motherhood, the maternal and fetal mortality among that group is significantly lower than in societies with a low incidence of late motherhood [2]. We conclude after a careful review of the literature that women entering motherhood late in life but with few other risks have good pregnancy outcome, although they are still subject to greater risks compared with younger women.

Those differences arise, *inter alia*, from the fact that as the age at pregnancy increases so does the rate of medical and surgical disease; that is, there is a greater incidence of cardiovascular, metabolic, renal, oncological, and autoimmune diseases. A large population-based study [11] demonstrated in the case of pregnancy after age 40 years, above all, an increased rate of cesarean delivery (primiparous age 40=47% vs. age 20–29=23%), an increased incidence of intrauterine growth restriction (primiparous age 40=3% vs. age 20–29=1%), an increased incidence of gestational diabetes (primiparous age 40=7% vs. age 20–29=2%), and a shorter pregnancy term (primiparous age 40=273 days vs. age 20–29=278 days). Other studies have drawn attention to the greater incidence of pre-eclampsia, the greater incidence of postpartum bleeding, and the increased number of multiple pregnancies.

There have been calls for more intense and complete level of preconception care and counseling [4, 6–8]. On the basis of preventive concern for the child, previous studies have recommended the taking of periconceptional folic acid to encourage vaccinations before pregnancy, and in the case of chronic diseases the adjustment of treatment strategies to reflect the planned pregnancy.

Pregnancy at the end of the reproductive cycle represents a major test to the multiple organ systems of the potential mother. Thus, successful late motherhood depends on the availability and the activation of physical resources. Timely preventive measures may help avoid the depletion of such resources as well as their replenishment.

The recommendation given to women, in the context of family planning counseling, of not delaying their pregnancy is often unrealistic. As a result, the aim of family planning counseling seeking to ensure low-risk and successful pregnancies with a positive outcome should be to recommend to women preventive measures that contribute to a favorable pregnancy and birthing process at a later age. Compelling evidence for such counseling has not been fully established. In this context, the age of the father and the quality of his

semen are important and were not valued highly. However, both practice and research offer support for this approach.

Possible preventive measures

Evidence (or lack thereof) is rare from preventive areas, such as nutrition recommendations. Other factors, such as micro-nutrients, alcohol consumption, smoking, vitamin D intake, omega fatty acids, estrogen levels, stress, and sports are reviewed and put in context here.

An important preventive measure that can be taken before pregnancy is to observe a healthy and balanced diet consisting of 20% protein, 35% fat, and 45% carbohydrates, as well as to avoid excess weight. Women who are overweight and obese are more likely to experience complications, such as cardiovascular disease, diabetes mellitus type 2, and hypertension. Preventive action should include adoption of a diet reflecting the food pyramid and the avoidance of excess weight and obesity [16]. Intervention studies involving weight reduction before pregnancy suggest a lowering of pregnancy risks for women who were previously obese [1] as the incidence of birthing complications, diabetes, and pre-eclampsia was reduced. It is recommended that women should aim for a body mass index between 20 and 25 [22, 23].

The question of whether deficiencies in micronutrients can exacerbate the aging process and if supplementation can delay such a process remains to be established by evidence-based research.

The prolonged consumption of high quantities of alcohol by women (more than 40 g/day over a long period) results in organic changes [9] that contribute to increased risks during pregnancy at any age.

Smoking causes considerable long-term harm to women's bodies [21]. This explains the well-respected and widespread recommendation not to smoke at any time.

Women of reproductive age who wish to have a child may be advised to take vitamin D supplements (400 IU vitamin D daily), *inter alia*, with a view of increasing the likelihood that a subsequent pregnancy will result in a successful spontaneous delivery [12]. For a definitive assessment of that recommendation, detailed observational studies are needed, focusing on vitamin D levels in non-pregnant women, the progress of their subsequent pregnancy, and fetal outcome.

The concentration of unsaturated fatty acids in tissues is important for healthy development [14, 15, 18, 19]. At present, there are no intervention studies under way in connection with the issue addressed in our paper. For that reason, no recommendations can be given. However, evidence concerning the resolution of mucosal inflammatory responses orchestrated by chemical mediators [20] would suggest that useful findings might follow.

From the very beginning of life, estrogens are crucial for the development of many features of the human organism [10]. It is unknown whether estrogen substitution in women

who enter motherhood late in life would produce protective effects in that regard. The authors are unaware of any clinical studies on that question. However, molecular cell culture studies appear to support the hypothesis [25].

Conclusions

Research on environmentally induced biological changes during aging—that is, focusing on the organism's adaptive plasticity [24]—is particularly crucial to this area especially with regard to the pathophysiology and prevention of age-related diseases (e.g., high blood pressure or diabetes).

Compared to behavioral sciences and neurosciences [e.g., [26] [27]], the notion of facilitating positive plasticity seems underdeveloped in medical research. Human development and aging are not determined but rather are the result of continuous interactions between biology, context, and the aging individual [3]. Thus, it is of utmost importance to explore the conditions under which developmental potential can be activated. It is known that this plasticity is greatest at the beginning of the lifespan and decreases thereafter. However, some plasticity is maintained until death unless a severe pathology intervenes. In this context, the notion of “the cell as a memory storage of environmental signals” is extremely attractive for medical research [13]. More systematic knowledge is necessary about the historical changes in vital parameters in order to learn about the biological difference between succeeding cohorts.

The current state of research also lacks evidence-based findings that demonstrate links between epigenetic events and age-related phenotypic phenomena. However, in the light of the considerable research in this area, it is increasingly recognized that the epigenome is plastic and that this plasticity is at its greatest when the organism is young. Nonetheless, the extent to which targeted environmental measures can be used as epigenetic events and thus influence the phenotype in the desired manner remains largely speculative. Thus, considerable research is still required both on the physiological changes in the body and on the possibilities to exert a preventive influence. For example, we propose that physiological changes in the Doppler flow patterns in the uterine arteries be examined with reference to a woman's age and her preexisting diseases and following preventive action. Also, it would be highly recommendable to very closely investigate women who successfully gave birth to a child rather late in life in order to derive further ideas about the conditions, and their interactions, that might foster the success of late childbearing. Subsequently, controlled clinical studies testing such hypotheses need to follow.

In all areas, recommendations should take account of the fact that fertility decreases with age. Whereas in the case of 20–24-year-old women seeking to have a child, some 90% will become pregnant within a year, in the case of 30–39-year-olds that figure drops to 50%. Whether that percentage

is likely to change in the future, in light of the suggestions advanced in this article, remains entirely open.

References

- [1] Amann-Gassner U, Hauner H. Adipositas vor und während der Schwangerschaft. Möglichkeiten der Ernährungstherapie. *Adipositas*. 2007;1:17–24
- [2] Anthony S, Jacobusse GW, van der Pal-de Bruin KM, Buitendijk S, Zeitlin J, EURO-PERISTAT Working Group on Risk Factors. Do differences in maternal age, parity and multiple births explain variations in fetal and neonatal mortality rates in Europe? – Results from the EURO-PERISTAT project. *Paed Perinat Epidemiol*. 2009;23:292–300
- [3] Baltes PB, Lindenberger U, Staudinger UM. Lifespan theory in developmental psychology. In: Lerner RM, editor. *Handbook of child psychology*. 6th ed. Vol 1. New York: Wiley; 2006. p. 569–664
- [4] Berghella V, Buchanan E, Pereira L, Baxter JK. Preconception care. *Obstet Gynecol Surv*. 2010;65:119–31
- [5] Blickstein I. Motherhood at or beyond the edge of reproductive age. *Int J Fertil Womens Med*. 2003;48:17–24
- [6] Cefal RC, Moos, MK. *Preconceptional health care – a practical guide*. St. Louis, MO: Mosby; 1995
- [7] Dudenhausen JW. Früherkennung und beratung vor der Schwangerschaft: Prägravid Risiken. Frankfurt: Umwelt&Medizin; 1995
- [8] Dudenhausen JW, Friese K, Kirschner W. Präkonzeptionelle Gesundheitsberatung und Beratung zur Wahl der Geburtsklinik als weitere Instrumente zur Verringerung von Frühgeburten. *Z Geburtsh Neonatol*. 2007;211:142–6
- [9] Foerster M, Marques-Vidal P, Waeber G, Vollenweider P, Rodondi N. Association between alcohol consumption and cardiovascular risk factors: a narrative review. *Rev Med Suisse*. 2010;6:505–6
- [10] Genazzani AR, Pluchino N, Luisi S, Luisi M. Estrogen, cognition and female ageing. *Hum Reprod Update*. 2007;13:175–87
- [11] Gilbert WM, Nesbitt TS, Danielsen B. Childbearing beyond age 40 years: pregnancy outcome in 24,032 cases. *Obstet Gynecol*. 1999;93:9–14
- [12] Ginde AA, Sullivan AF, Mansbach JM, Camargo CA Jr. Vitamin D insufficiency in pregnant and non-pregnant women of childbearing age in the United States. *Am J Obstet Gynecol*. 2010;202:436–8
- [13] Groom A, Elliott HR, Embleton ND, Relton CL. Epigenetics and child health: basic principles. *Arch Dis Child*. Epub 2010 Aug 16
- [14] Hadders-Algra M, Bouwstra H, van Goor SA, Dijck-Brouwer DA, Muskiet FA. Prenatal and early postnatal fatty acid status and neurodevelopmental outcome. *J Perinat Med*. 2007;35:S28–34
- [15] Hadders-Algra M. Prenatal long-chain polyunsaturated fatty acid status: the importance of a balanced intake of docosahexaenoic acids and arachidonic acid. *J Perinat Med*. 2008;36:101–9
- [16] Jungheim ES, Moley KH. Current knowledge of obesity's effects in the pre- and periconceptional periods and avenues for future research. *Am J Obstet Gynecol*. 2010;203:525–30
- [17] Karl K, Lack N. Die ältere Erstgebärende – wie hoch ist das Risiko wirklich? *Die Hebamme*. 2009;22:234–7
- [18] Koletzko B, Larque E, Demmelmair H. Placental transfer of long-chain polyunsaturated fatty acids (LC-PUFA). *J Perinat Med*. 2007;35:S1–11
- [19] Koletzko B. Prenatal supply of docosahexaenoic acid (DHA): should we be worried? *J Perinat Med*. 2008;36:265–7
- [20] Levy BD. Resolvins and protectins: natural pharmacophores for resolution biology. *Prostagl Leukot Essent Fatty Acids*. 2010;82:327–32
- [21] Pelkonen M. Smoking: relationship to chronic bronchitis, chronic obstructive pulmonary disease and mortality. *Curr Opin Pulm Med*. 2008;14:105–9
- [22] Plagemann A, Dudenhausen JW. *Adipositas als Risiko in der Perinatalperiode*. Munich: Springer; 2010
- [23] Plagemann A, Roepke K, Harder T, Brunn M, Harder A, Witrock-Staar M, et al. Epigenetic malprogramming of the insulin receptor promoter due to developmental overfeeding. *J Perinat Med*. 2010;38:393–400
- [24] Solomons NW. Developmental origins of health and disease: Concepts, caveats, and consequences for public health nutrition. *Nutr Rev*. 2009;67(Suppl 1):S12–6
- [25] Simoncini T, Caruso A, Giretti MS, Scorticati C, Fu XD, Garibaldi S, et al. Effects of dydrogesterone and of its stable metabolite, 20- α -dihydrodydrogesterone, on nitric oxide synthesis in human endothelial cells. *Fertil Steril*. 2006;86(Suppl 4):1235–42
- [26] Staudinger UM, Marsiske M, Baltes PB. Resilience and reserve capacity in later adulthood: potentials and limits of development across the life span. In: Cicchetti D, Cohen D, editors. *Developmental psychopathology*. 2: Risk, disorder, and adaptation. New York: Wiley; 1995. p. 801–47
- [27] Voelcker-Rehage C, Godde B, Staudinger UM. Cardiovascular and coordination training differentially improve cognitive performance and neural processing in older adults. *Front Hum Neurosci*. 2011;5:1–12

The authors stated that there are no conflicts of interest regarding the publication of this article.

Received August 16, 2011. Revised August 30, 2011. Accepted August 31, 2011. Previously published online November 3, 2011.