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Do menopause and natural embryo selection support human species evolution and development?

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SUMMARY

It is a well-known fact that elderly women are in higher risk of having children with inherited defects of various etiologies. The precise reasons for this phenomenon are unknown. One of embryological hypotheses tries to explain this fact. During oogenesis, germ line cells are formed during prenatal life and remain in cytological stability in postnatal life. This is when the mutations caused by environmental and endogenous factors accumulate and deteriorate their genetic quality. Furthermore, the predetermination of cell numbers during prenatal life limits future reproductive capabilities of women. These facts underlie the "evolutionary grandmother hypothesis" which explains the peculiarity of women's reproduction. According to this hypothesis, elder women give up their reproduction to take care of related children. Recently, attention has been paid to progressing decline in the interaction between the mother and fetus in older women. It consists in the impairment of mechanisms that regulate natural intrauterine selection of defected fetuses. As a result, enhanced maternal tolerance to abnormal embryos is observed. These observations define the "closed door hypothesis" and clarify higher incidence of inherited defects in children of elderly women.

Key words: menopause; evolution; inherited defects; late motherhood

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INTRODUCTION

The basic biological task of each organism is reproduction, i.e. producing healthy offspring and passing on one's own genes to the subsequent generation and enabling them to spread in the genet0ic pool of the population. Each individual aims at reproduction and makes every effort to enable it, leading to having numerous offspring. This is the basic law of evolution, true for all species, including humans. However, errors in biological processes do happen during fertilization as well as embryonic and fetal development. They result in developmental anomalies and production of a child with an inherited defect. In humans, major congenital anomalies, which limit the comfort of life, occur in approximately 3% of live births. Even 1/3 of them can constitute a direct threat to life of a neonate or deteriorate health and disable future reproductive capabilities. At the same time, minor malformations are estimated to occur in even 15% of neonates and are no usually lethal. The direct etiology of most of these defects remains unknown despite the development of medicine, biology and particularly cytogenetics, molecular biology and experimental embryology that uses animal models of human disease entities. It has been estimated that approximately 85% of defects of a known mechanism of occurrence depend on genetic factors. 6% of them are caused by chromosome aberrations, 7.5% by genetic mutations and 20% can be explained with mixed genetic and environmental causes. Maternal diseases and infections during pregnancy constitute 3.5%, 1.5% result from drug, alcohol or radiation exposure, and the etiology of the remaining cases is unclear [1,2]. Errors during fertilization and embryogenesis are much more common than people generally think. It is currently believed that approximately 90% of abnormal embryos or fetuses with anomalies die and

undergo spontaneous elimination or miscarriage. This usually happens without any significant symptoms or consequences for the mother's health and her future reproduction. Mechanisms of this natural, biological selection remain unknown, but its occurrence has a significant influence on evolution and directly affects the health of the population [2].

A well-known fact, which is difficult to explain, is the strong will to have one's own children combined with the need to specify family connections (e.g. fatherhood) that bind parents and their offspring. This is referred to as strong maternal or paternal instinct, whereas given biological behaviors and social norms enable proper care of children. Such behaviors are commonly referred to as family bonds or, in more biological terms, own gene promotion. This is not only an expression of social needs, but also a proof of the unity of humans with the living world and the fact that a human being is also subject to evolution laws. One might also risk a statement that strengthening biology with this manner of social behavior has facilitated the development of the human species, resulting in obtaining such a high status among living organisms. Humans are the only species that is subject to both biological and social evolution.

THE PHENOMENON OF MENOPAUSE

The notion of evolution seems to be significant in research on certain aspects of human reproductive biology, particularly physiological processes typical of female biology that are so unique among mammals. One of them is the presence of menopause, which is singular among female mammals. Menopause is the loss of ovarian function entailing the loss of fertility and the impossibility of having children long before death. This phenomenon is undoubtedly caused by, among others, atypical and rapid increase in average life expectancy and a delay of biological ageing in people caused by advancements in the field of medicine. On the other hand, the evolutionary role of women incapable of reproduction but actively looking after children of younger mothers, frequently relatives, has grown. As a result, this has led to own gene promotion. This view is referred to as the "evolutionary grandmother hypothesis" in which the relevance of family in child care and developing family bonds play a crucial role [3–5].

The basic medical hypothesis explaining the relationship of maternal age with fetal pathologies concerns the atypical course of gametogenesis in a woman. In humans, mitotic divisions of germ line cells lead to the development of a specified maximum number of oogonia (primordial gametes) which begin their meiotic divisions at about 4 months of prenatal life. As a result, the number of potential germ line cells that could transform into mature oocytes capable of fertilization is determined early and does not increase postnatally. Moreover, the number of oogonia depletes rapidly mainly due to physiological and genetically determined cell death, i.e. apoptosis [6,7]. The natural loss of reproductive capabilities during menopause results from depletion of precursor cell reserves. It seems that the moment of meiosis initiation in the prenatal ovary development is the time during which there is the greatest number of precursor cells of female gametes (approximately 9,000,000 prophase primary oocytes). From this moment on, oocytes can disappear due to apoptosis, which leads to their reduction to approximately 1,000,000 cells at birth. This process depends on a genetic mechanism regulating apoptosis, e.g. on the activity of various genes [4]. Primordial follicles, in which oocytes will develop further until ovulation, begin to form around prophase oocytes in the prenatal life. Various histological observations conducted on different mammalian species and humans indicate that the number of ovarian follicles, and consequently also oocytes, is prenatally predetermined. It is not possible for them to appear or replenish during the mature life. This idea appeared in the 1950s and became finally established in the 1960s. It seems to be one of the dogmas of human and mammalian development.

This model of oogenesis and fertility of women is one of the factors underlying an increasing risk of having a child with a congenital defect in older women. Women conceiving at an older age (the age of 35 is considered critical) statistically more frequently present with pregnancy and childbirth disorders, and have children with symptoms of severe pathological syndromes. They can results from genetic causes: trisomies and structural chromosomal aberrations as well as genetic mutations [10,11].

Potential gametes, oocytes that appeared and started meiosis in the prenatal period, remain dormant for most of the woman's life. They do not undergo cell divisions during which they would be selected in terms of genetic material correctness. At the same time, these cells are

exposed to unfavorable biochemical substances, which appear due to systemic and physiological processes, as well as mutagenic environmental factors resulting in the development and accumulation of mutations in their genetic material. Random accumulation of genomic mutations in oocytes is referred to their genetic ageing. As a result, the probability of a genetic abnormality of gametes rises with the woman's age. This can negatively affect the development of embryos after fertilization of oocytes that have been waiting for too long [1,11,12].

SELECTION PROCESS

A simple statistical elucidation of deteriorating health of children born from an older mother is not the only theory explaining this fact. It must be remembered that cellular mutations are random and can occur in germ line cells at any time during oogenesis. However, it has been demonstrated that the maternal organism is capable of selection and elimination of damaged and abnormally developing fetuses. This process is highly effective and concerns most developmental anomalies. Nevertheless, a recently formed theory states that this ability is variable. According to this theory, selection processes eliminating abnormally developing fetuses weaken with the future mother's age due to impaired mother–fetus communication. This results from a change in the reproductive selection strategy caused by losing reproductive capabilities with age. Due to various physiological mechanisms, the organism of a woman nearing menopause gradually increases tolerance to pathological embryos. This hypothesis is referred to as the "closed door hypothesis." It correlates with biological effects underlying the "grandmother hypothesis." These two theories together elucidate the basis of biological deterioration of fertility in older women and explain evolutionary relevance of this phenomenon [13,14,15].

CONCLUSION

In the recent years, scientists and societies have been increasingly concerned about the separation of humans from the laws of nature caused by the development of technology and medicine as well as a rapid pace of socioeconomic and environmental changes. Moreover, the development of medicine and broadly understood health care can hold some dangers. For instance, it can lead to the deterioration of the genetic condition of ageing populations. Preventive measures undertaken to save the life of neonates with severe developmental defects at all costs, although they are just from the humanistic point of view, can have biological consequences in the form of promoting and increasing unfavorable genes in the genetic pool of our species. Moreover, delayed motherhood can also contribute to such outcomes. However, in the light of modern population genetics research, this does not significantly affect the occurrence of unfavorable alleles in the genetic pool, but merely constitutes a transient disorder. This is associated with the fact that individuals with such genes frequently do not reproduce and do no pass these genes to future generations. However, whether this view is justified from the point of view of contemporary medicine, biology, genetics, evolutionism and anthropology remains unclear and only subsequent years will bring answers to this question [16–18].

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