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Effects of age on male fertility

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Later parenting is considered by many to have advantages, parents-to-be may feel themselves more stable to rear children. In addition, many men start a second family later in life. Thus, paternal age becomes an emerging issue. Aging affects male fertility by a scope of factors, which are not fully understood to date. Generally, the amount of produced sperm cells as well as their motility decreases with age, as testicular histological architecture deteriorates. Decreased fecundity and an increased risk for disturbed pregnancies occur with advancing paternal age. Some rare autosomal dominant pathologies are clearly related to paternal age. Altered patterns of epigenetics/gene expression in aging sperm seem to affect a range of neurocognitive disorders and also metabolic dyshomeostasis across generations. Such effects refer to men older than 40 years and may have impact on socioeconomic issues. Nevertheless, councelling of older men seeking paternity should be patient-oriented and weigh statistical probabilities against the right for individual life-planning.

Introduction

Parenthood is a joy, a privilege and also a commitment and obligation that comes in many forms at different ages and stages of life. With the decision to become firmly established in a career before bringing children into the world, more and more parents are choosing to wait until later in life to

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become first time parents. Waiting until the age of forty or beyond to become a parent bears unique advantages and disadvantages.

This attitude is due to social phenomena such as a general rise in life expectancy and social possibilities for women to pursue their professional career, as well as the use of various methods of contraception, and it has contributed to delaying family planning and parenthood up to the mid or late thirties of women. Assisted reproductive technologies have become accessible to a wide population and enabled couples to become parents later in life. Later parenting is considered by many to have advantages for parents, who may feel themselves more stable, financially and emotionally, to rear children. Simultaneously, it is well established that the main limiting factor to fertility and healthy reproductive outcome with an older couple is women's age [1,2].

Hence, the questions arises to what extent also paternal age influences the course of pregnancy and, most of all, the health of the child. Male fertility persists in general with advancing age [3], and many men adopt the idea of founding a second family later in life, with a new and/or younger partner. Thus, a trend of older parenthood is true also for males, not only women. In England, for example, the rate of fathers aged 35–54 years has increased from 25% to 40% within the recent years [4].

Consequently, attention has to be paid to the influence of advanced paternal age on reproductive outcome. Increasing evidence shows that advanced paternal age is associated with changes in various reproductive functions: beginning with the production of gonadotropins, sexual functions in general, semen production, fertility, pregnancy outcome and ending with the incidence of birth defects and diseases in offspring. There is an increasing body of evidence that paternal age is linked to genetic fragility transported by sperm DNA, having impact on the offspring at the embryonic, fetal or perinatal level as well as later in life [5].

This emerging concern has to be weighed against the calculated risk for the actual occurrence of an adverse effect in offspring, and it has to be considered to what extent knowledge about paternal effects due to aging should influence counseling processes of couples seeking fertility treatment.

Sexual functions of the aging male in general

Male sexual dysfunction in infertile couples is nowadays, given the possibilities of assisted reproductive methods and other treatment options, rarely the reason for infertility, but rather it is more often caused or aggravated by the fact of infertility and its own psychological implications [6]. In general, male sexual dysfunction, especially when age-related, is mostly due to co-morbidities, namely obesity, arterial hypertension, type 2 diabetes mellitus and late-onset hypogonadism [7–9]. Thus, albeit sexual dysfunction is more prevalent in couples of advanced age [10,11], it can also be present in middle-aged couples who often still seek paternity, as the above-named morbidities present with increasing prevalence also in relatively younger men [7,12].

Reflecting the multifactorial causes, therapy options for male sexual dysfunction are broad. They include psychosocial interventions, but mainly drug interventions, such as with phosphodiesterase inhibitors for erectile dysfunction or dapoxetine for premature ejaculation [13,14]. Sexual dysfunction itself has no known influence on germ cells and its impact on infertility can be overcome by measures of assisted reproduction. The use of phosphodiestarse-5 inhibitors may even promote sperm motility and they can be used by (older) men with erectile dysfunction and the wish for paternity [15].

On the other hand, the use of 5-alpha-reductase inhibitors for treatment of male pattern baldness or benign prostate hyperplasia, reducing serum concentrations of dihydrotestosterone, cannot only lead to diminished sexual functions (mainly decreased libido and impaired erectile capacity) [16], but they may also induce lower semen volume and decreased sperm motility [17]

Testicular function, spermatogenesis and ejaculate parameters in relation to age

Male age is associated with a thickening of the basal membrane of seminiferous tubuli, in parallel with reduction of the seminiferous epithelium and reduced vascularization of the testes. This has, most likely, an impact on histological architecture: a reduced number of Sertoli cells and Leydig cells [18]. This explains the age-related decline in daily sperm production per testis in a much earlier study [19].