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# Artemis Saage

# Late Mothers: Pregnancy 40+ and Getting Pregnant Faster

A Practical Guide for Women on Fertility, Late Birth, Medical Support, and Life Balance After 40

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## **Imprint**

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Parents over 40+: The Practical Guide to Late Motherhood

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Parents over 40+: The Practical Guide to Late Motherhood

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#### Introduction

To provide you with the best possible reading experience, we would like to familiarize you with the key features of this book. The chapters are arranged in a logical sequence, allowing you to read the book from beginning to end. At the same time, each chapter and subchapter has been designed as a standalone unit, so you can also selectively read specific sections that are of particular interest to you. Each chapter is based on careful research and includes comprehensive references throughout. All sources are directly linked, allowing you to delve deeper into the subject matter if interested. Images integrated into the text also include appropriate source citations and links. A complete overview of all sources and image credits can be found in the linked appendix. To effectively convey the most important information, each chapter concludes with a concise summary. Technical terms are underlined in the text and explained in a linked glossary placed directly below.

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# 1. 0. 0. Desire to Have Children and Fertility after 40

he desire to have children after 40 raises many questions: How significantly does fertility actually decline with increasing age? What biological processes are involved? And what options does modern medicine offer to realize the dream of having one's own child even at an advanced age? Family planning is increasingly being postponed in our society. Career, partner choice, and personal development lead many individuals to consider having children only later in life. At the same time, the biological clock is ticking—both for women and men, albeit to different extents. This chapter explores the complex hormonal and biological changes that accompany aging. It presents evidence-based strategies for optimizing fertility and provides an overview of current treatment options in reproductive medicine. It becomes clear that while a late desire for children poses a particular challenge, it is no longer an impossibility thanks to modern medicine. The following pages offer wellfounded information for all those dealing with the topic of wanting children after 40—whether as directly affected individuals or as medical professionals supporting couples on this journey.



## 1.1.0. Biological Foundations

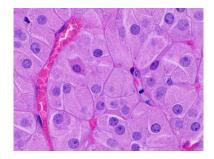
he biological processes that determine our fertility are complex and dynamic. What happens in our bodies as we age? What hormonal changes affect our reproductive capacity after 40? And how does age specifically impact the quality of eggs and sperm? In recent years, science has gained significant insights into the biological foundations of fertility in advanced age. From the molecular level to the visible effects on reproductive ability, a nuanced picture of age-related changes emerges—both in women and men. These findings are not only important for understanding one's own fertility but also form the basis for modern treatment approaches and preventive measures. A solid understanding of the biological foundations allows for the development of realistic expectations and informed decision-making. The following sections will illuminate the key aspects in detail.

"From the age of 37, the decline in egg cells accelerates significantly, which has far-reaching consequences for fertility."

# 1. 1. Hormonal Changes with Age

s individuals age, both men and women undergo significant hormonal changes that can affect various aspects of their health and well-being. These changes impact three key hormonal systems: sex hormones (estrogen and testosterone), dehydroepiandrosterone, and the growth hormone/insulin-like growth factor I axis [s1].

In men, the hormonal aging process begins gradually. After the age of 30, testosterone levels decline by 1-2% annually [s2]. This phase, referred to as andropause, typically manifests in the late 40s to early 50s [s3]. A particularly important aspect is the decrease in Leydig cells in the testes men over 40 may experience a reduction in their number by up to 44% [s2]. This leads to decreased testosterone production. increasing further exacerbated by insensitivity of the hypothalamic-pituitarytesticular axis.



Leydig cells [i1]

Symptoms of andropause can be diverse and usually develop gradually. Affected men often report:

- Loss of libido and erectile dysfunction
- Decrease in muscle mass alongside an increase in body fat
- Mood swings and depressive symptoms
- Reduced vitality and lack of motivation
- Sleep disturbances and concentration difficulties [s3] [s2]

It is important to note that approximately 90% of cases of erectile dysfunction are attributable to medical issues rather than aging itself [s4]. Regular medical check-ups are advisable to distinguish between age-related changes and treatable conditions. In women, the hormonal aging process differs from that in men. Menopause, which typically occurs between the ages of 45 and 55, marks the end of reproductive years [s5]. This phase is characterized by the loss of ovarian follicular function and a significant decline in estrogen levels. The transitional phase, known as perimenopause,

can extend over several years and brings various physical and emotional changes.

Typical symptoms of menopause include:

- Hot flashes and night sweats
- Irregular menstrual cycles
- Vaginal dryness
- Sleep disturbances
- Mood swings [s5]

A particularly important aspect of hormonal aging is its impact on bone health. The lack of estrogen during menopause can lead to accelerated bone density loss, increasing the risk of osteoporosis [s5]. Regular bone density measurements and adequate calcium and vitamin D intake are therefore especially important.

For both genders, a healthy lifestyle can positively influence the effects of hormonal changes. Recommended practices include:

- Regular physical activity to maintain muscle strength and bone density
- A balanced diet with sufficient proteins and essential micronutrients
- Stress management and adequate sleep
- Regular medical check-ups

The molecular mechanisms of aging are increasingly well understood. Studies have shown that during testicular aging, over 1500 mRNAs and 715 lncRNAs exhibit changes in their levels [s6]. This improved understanding of the underlying mechanisms could lead to more targeted treatment approaches in the future. It is important to emphasize that hormonal changes with age are a natural process that can vary significantly among individuals. While some people develop pronounced symptoms, others may navigate this phase with minimal discomfort. Open communication with a physician and consideration of therapeutic options can help maintain quality of life during this transitional phase.

### Glossary

#### **Andropause**

Also known as 'male menopause', this phase describes the hormonal adjustment in men, typically occurring between the ages of 40-60, characterized by a reduced production of the male hormone testosterone.

#### Dehydroepiandrosterone

A hormone produced by the adrenal cortex that serves as a precursor for the production of sex hormones, with levels continuously decreasing from the age of 25.

### **Leydig Cell**

Specialized cells in testicular tissue responsible for the production of the male sex hormone testosterone and other important hormones.

#### **IncRNA**

Long non-coding ribonucleic acids that perform important regulatory functions in the cell and can control gene activity.

#### **mRNA**

Molecules that transport genetic information from the cell nucleus to the ribosomes, where they serve as blueprints for protein synthesis.

### Perimenopause

The time before actual menopause, which can last from 2 to 8 years, during which the female body begins to adjust hormone production.

# 1. 1. 2. Egg Quality and Fertility Window

he biological clock ticks inexorably for women - even before birth, the maximum number of eggs is determined. The peak of the egg supply is reached in the 20th week of pregnancy, after which a continuous decline begins [s7]. From the age of 37, this process accelerates significantly, which has far-reaching consequences for fertility [s7]. Egg quality is determined by two crucial factors: quantity (the number of remaining eggs) and quality (developmental potential) [s8]. Particularly, the quality of eggs decreases with advancing age. This is evidenced by an increased rate of chromosomal abnormalities (aneuploidies) - for women over 40, the risk is ten times higher than for 25-year-olds [s7]. The molecular mechanisms behind this decline in quality are diverse: DNA damage accumulates, mitochondrial function deteriorates, and changes occur in protein expression [s9]. A recently identified key gene called TOP2B plays an important role - its reduced activity leads to developmental disorders in early embryos [s9]. For women wishing to conceive, this means: The best chances for a successful pregnancy exist in the early 20s [s10]. From the age of 35, women who do not become pregnant within 6 months should seek a specialized fertility clinic [s7]. For women over 40, the success rates with conventional treatments are significantly reduced here, in vitro fertilization (IVF) may be the better option [s11].

Practical measures can positively influence egg quality:

- An omega-3-rich diet has been shown to be beneficial in studies, while a high proportion of omega-6 fatty acids shows negative effects [s12].
- Antioxidants can reduce oxidative stress, which impairs egg quality [s13].
- Special supplements can support mitochondrial function [s14].

The <u>ovarian reserve</u> can be assessed through various tests, with the <u>anti-Müllerian hormone</u> (AMH) being considered the most reliable marker [s10]. However, it is important to know: These tests provide more information about quantity than about quality of the eggs [s8]. A high AMH level may increase the chance of more transferable embryos per IVF cycle, but it does not guarantee a successful pregnancy [s15]. For women over 40, egg donation often represents the most effective treatment option [s11]. The pregnancy rates are significantly higher than when using one's own eggs. However, this option should be carefully considered and requires thorough

counseling. Particular attention should be paid to the prevention of DNA damage. Oxidative stress, which is particularly elevated in women with endometriosis, can further impair egg quality [s13]. Modern techniques such as preimplantation genetic testing (PGT-A) can help identify chromosomally normal embryos, thereby improving the chances of success [s13]. The declining fertility with age is a complex interplay of various factors. In addition to egg quality, the general health status and the functionality of the reproductive organs also play an important role [s10]. Early engagement with the topic of desire for children and, if necessary, preventive measures such as social freezing can make family planning more flexible.

### Glossary

### Aneuploidy

A change in the number of chromosomes, where individual chromosomes are missing or present in excess. This can lead to developmental disorders or miscarriages.

#### **Anti-Müllerian Hormone**

A hormone produced by the ovaries that serves as a biomarker for a woman's remaining egg reserve. The higher the value, the greater the egg reserve.

#### **Ovarian Reserve**

The total supply of eggs in a woman's ovaries that is available for future pregnancies.

## **Social Freezing**

The precautionary freezing of unfertilized eggs at a younger age to use them for pregnancy at a later time.

# 1. 1. 3. Male Fertility in Advanced Age

n contrast to female fertility, which is marked by a clearly defined end to reproductive capability, the decline in male fertility occurs gradually and less obviously. Nevertheless, scientific studies show significant age-related changes in sperm quality that are relevant for men wishing to have children later in life [s16]. From around the age of 35, measurable changes in sperm parameters begin. The volume of ejaculate continuously decreases, with a particularly noticeable decline starting at 35.5 years [s16]. Concurrently, other important parameters such as sperm count, motility, and morphology also deteriorate. Sperm motility decreases by approximately 1.2% per five years of life [s16]. The molecular changes in the sperm of older men are particularly significant. DNA integrity declines with age, which is reflected in increased **DNA** fragmentation [s17]. Men over 40 exhibit a significantly higher rate of DNA damage in their sperm compared to younger men—the risk is more than double [s18]. These damages primarily arise from oxidative stress and reduced DNA repair capacity. A fascinating aspect is the epigenetic changes in the sperm epigenome of older men. Studies have shown that these changes occur more frequently than genetic mutations [s19]. The altered methylation patterns primarily affect genes associated with the development of the nervous system, which may have implications for the health of offspring. For couples wishing to have children, these findings indicate that the age of the man should also be considered in family planning. The time until pregnancy increases with the man's age, and the risk of miscarriage rises [s20]. In assisted reproductive techniques such as in vitro fertilization, success rates decline with the increasing age of the man [s16].

Practical recommendations for men wishing to have children later in life:

- Regular sperm analyses starting at age 35 to monitor sperm quality
- Reduction of oxidative stress through a healthy diet and lifestyle
- Avoidance of factors that can further impair sperm quality, such as smoking, excessive alcohol consumption, and obesity [s21]

Societal developments show a clear trend towards later fatherhood [s22]. This trend is facilitated by various factors such as increased life expectancy, widespread use of contraceptives, and late marriages. For men wishing to have children, it is important to know that while fertility does not abruptly

end, sperm quality and thus the chances of a successful pregnancy decline with age. Interestingly, studies also show correlations between paternal age and the health of offspring. Children of fathers over 40 have an increased risk of certain developmental disorders, although the absolute risk for the individual remains low [s23] [s20]. For optimal family planning, early engagement with the topic of fertility is advisable. Men planning for late fatherhood should be aware of the potential challenges and consider preventive measures such as <u>cryopreservation</u> of sperm at younger ages.

## Glossary

### Cryopreservation

A method for long-term storage of biological material by freezing at very low temperatures, usually in liquid nitrogen at -196°C.

## **DNA Fragmentation**

A process in which the genetic information in sperm breaks into smaller pieces, impairing sperm quality and fertilization ability.

## **Methylation Patterns**

Specific chemical markings on DNA that can act like a molecular switch to regulate gene activity.

### **Sperm Analysis**

A standardized laboratory examination to assess various quality characteristics of sperm such as count, shape, and motility.

## **Sperm Epigenome**

The totality of all chemical markings on the DNA of sperm that regulate gene activity without altering the DNA sequence itself.

## **Summary - 1.1. Biological Foundations**

- Testosterone production in men decreases annually by 1-2% after the age of 30.
- In men over 40, the number of Leydig cells is reduced by up to 44%.
- 90% of cases of erectile dysfunction have medical causes and are not age-related.
- During testicular aging, over 1500 mRNAs and 715 lncRNAs show changes.
- The ovarian reserve peaks at the 20th week of pregnancy.
- In women over 40, the risk of chromosomal abnormalities is ten times higher than in 25-year-olds.
- The gene TOP2B plays a key role in developmental disorders of early embryos.
- A diet rich in omega-3 improves egg quality, while omega-6 fatty acids have negative effects.
- Anti-Müllerian hormone (AMH) is considered the most reliable marker for ovarian reserve.
- Ejaculate volume begins to significantly decrease from the age of 35.5.
- Sperm motility decreases by 1.2% every 5 years of life.
- Men over 40 have twice the risk of DNA damage in sperm.
- Epigenetic changes in the sperm epigenome occur more frequently than genetic mutations.
- Altered methylation patterns particularly affect genes involved in nervous system development.



## 1. 2. 0. Fertility Optimization

ptimizing fertility after 40 presents unique challenges for many individuals. How can natural fertility be best supported during this life stage? What role do nutrition, exercise, and other lifestyle factors play? While the biological clock cannot be stopped, scientific studies indicate that targeted lifestyle adjustments can positively influence the chances of pregnancy even in later years. The complexity of the topic raises further questions: Which specific measures are truly effective? How can these be sustainably integrated into daily life? And what individual factors must be taken into account? The following pages offer evidence-based strategies and practical recommendations specifically tailored to the needs of individuals over 40 who wish to have children. Current research findings show that even small changes can make a significant difference.

"A body mass index (BMI) between 18.5 and 30 is considered optimal for fertility."