



Stopping or even reversing the

# Biological Clock

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**I**t is widely known that women have a more dramatic age-related decline in fertility than men. Men make sperm continuously and are capable of conceiving children late in life, while women usually exhaust their supply of eggs (oocytes) by their early fifties. In addition, the quality of a woman's eggs declines before the supply is exhausted, which significantly reduces her chances of conceiving as she ages.

These factors create the sense that women have a reproductive biological clock, which ticks at different speeds in different women. Some women conceive easily up to the age of forty while others begin to have problems with egg quality or number in their late twenties or early thirties. The average age that women seek fertility assistance because of an aging biological clock is in their mid-thirties. Because we have no way to measure the speed of a woman's biological clock, deciding to delay childbearing is somewhat like playing Russian roulette with your fertility.

If you don't have plans to reproduce when you are young, it may be worth the investment to get a preconception evaluation and counseling. The cost of delaying childbearing could be an expensive path to parenthood or an unanticipated need to use donor eggs or adopt.

### **1. Egg Number**

The census of eggs in the ovaries is a remarkable story. Women have the greatest number of eggs in their ovaries about halfway through their mother's pregnancy, before they are born. One estimate is that a woman starts with about 20 million eggs at about 20 weeks into her own conception. From here forward the number of eggs begins to decline. By birth, approximately 95% of the eggs are gone and by puberty another 60% have "left the nest". A woman enters puberty with something like 400 thousand eggs, or about 2% of what she had at the outset. The average woman ovulates about 400 times in her reproductive window with hundreds of eggs disappearing each month.





The process of maturing an egg to the point of ovulation takes about 3 months. Once again attrition is at work, however, and only a small number of the eggs that begin the 3-month trek survive to enter the woman's recruitable pool. This number, referred to as the ovarian reserve, can range from 1 to over 30 recruitable eggs, with the average being a little over 10. Normally a woman's brain only makes hormone (FSH) long enough to recruit one or two eggs each month, so most of the eggs that enter the recruitable pool never complete the journey. This recruitable pool is a resource that fertility clinics can tap into if it is available.

The size of the recruitable pool can be estimated by doing an ultrasound to count antral follicles or by measuring the level of AMH in your blood. As a woman approaches the end of her egg supply, a low AMH level becomes associated with a higher FSH level, which indicates that the brain is beginning to have a hard time getting the ovaries to respond. Eventually the eggs supply is exhausted and a woman enters menopause. The average age of menopause is 51 but about 1% of the population has menopause before the age of 40.

## 2. Egg Quality

***The largest cause of early pregnancy loss is due to mistakes in cell division, which cause cells to end up with too many or too few chromosomes.***

All humans are relatively inefficient at reproduction, i.e. humans naturally have recurrent pregnancy loss. Fortunately, we are unaware of most of the pregnancy losses because they occur between the time that a woman ovulates and her next menstrual period. The largest cause of early pregnancy loss is due to mistakes in cell division, which cause cells to end up with too many or too few chromosomes.

First, let's review some elementary biology:

- Humans normally have 23 pairs of chromosomes that need to be copied and passed to their daughter cells with each cell division. This process of cell division is called mitosis and the cells are referred to as being diploid because the chromosomes all exist as pairs.





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- Eggs and sperm, referred to as gametes, go through a process of reducing their chromosome number to one of each through a process called meiosis. Cells that only have one of each chromosome are referred to as haploid. Mistakes in cell division can occur and result in the daughter cells having too many or too few chromosomes (aneuploidy), which is almost always lethal for the descendants of those daughter cells.
- If a cell line has three copies of one chromosome it is referred to as trisomy and if it has one copy of a chromosome then it is referred to as monosomy. The only aneuploid states that are compatible with survival into adulthood are either trisomy 21 (Down's syndrome) or aneuploid states that involve the sex chromosomes.
- The most common place where mistakes in cell division seem to occur in the early phases of forming a baby is in the process of egg meiosis, i.e. reducing its chromosome number so that it can combine with a sperm and end up with a diploid complement of chromosomes.

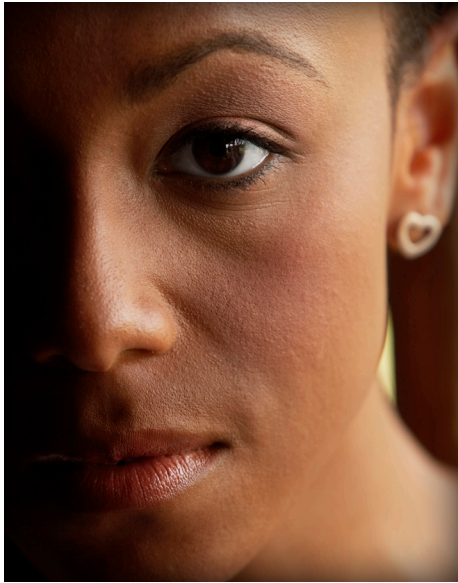
Remarkably, it has been estimated that at the age of 27, approximately 65% of human eggs are genetically abnormal and this percentage increases as we age. As a result, as many as 75% of pregnancies may abort spontaneously at the peak of human reproduction.

Approximately 75% of women who try to conceive when they are 30 will have a child within one year. This number declines to 66% at the age of 35 and 44% at the age of 40. However, women who show up in fertility clinics with unexplained infertility often have a more rapid decline in their fertility than the general population.

Why does egg quality decline with age? There is some exciting research that is revealing increasing evidence that the decline in egg quality with age is associated with a decrease in the number or quality of the mitochondria inside the egg. Mitochondria are organelles that live







inside cells and provide the energy that each cell needs to operate and divide. The question then arises as to how can we improve a woman's fertility through therapies that might increase the number or quality of the mitochondria in her eggs?

### 3. Intraperitoneal Environment

A woman's reproductive system sits in the lower part of her abdominal cavity and in close proximity with her urinary and digestive systems. Her eggs enter this cavity when she ovulates before they enter her fallopian tubes. There are some conditions, such as endometriosis, that are believed to create a hostile environment for eggs. Endometriosis is a natural consequence of menstruation and it is another fertility factor that increases as women age.

### 4. Preserving Fertility

If you are in your twenties or thirties, there are several steps you can take to slow down your biological clock and preserve your fertility, such as:

- Eating healthily
- Using hormonal contraceptives to decrease retrograde menstruation into the peritoneal cavity

All these things may improve your chances of conceiving later in life. There is a lot of research going on to determine how dietary factors (high carbohydrate diets, antioxidants, etc.) may influence general health as well as sperm and egg quality later in life.

If you know you won't be ready to have a baby for several years, freezing your eggs is also an option. Freezing your eggs before your fertility reaches its low point could improve your chances of parenting with your own eggs. If you have any questions about your fertility, consider meeting with a reproductive endocrinologist. Planning for pregnancy may save you a lot of money and anxiety later in life.

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## 5. Help with Conceiving

If you are already facing issues with the age-related decline in fertility, a reproductive endocrinologist has several tools to help you increase your chances of conceiving each month. There are many intermediate measures, but ultimately employing controlled ovarian hyperstimulation to tap into the ovarian reserve and protecting gametes through the process of in-vitro fertilization combined with aneuploidy screening is associated with the highest chance of conception and the lowest risk of multiple gestation. If there is a problem with both egg quality and egg numbers, oocyte donation is always available as a strategy to reverse the biological clock. Atlantic Reproductive Medicine Specialists have discovered that Research Triangle area is rich with young, educated women willing to serve as egg donors if other strategies have failed.



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## 6. What Does the Future Hold?

The field of assisted reproduction took off with the advent of in-vitro fertilization in 1978, and its frontiers have been pushed back at a steady rate ever since with the development of new drugs and technologies.

The ability to freeze eggs to stop the reproductive biological clock and preserve a woman's fertility has now entered the clinical armamentarium. Aneuploidy screening to increase the chances of conception and reduce miscarriage rates is available and hopefully will become less expensive in the coming months and years. Research efforts focusing on ways to slow down or reverse the aging process of eggs are happening as this is written. Coenzyme Q 10 has been demonstrated to enhance the fertility of several species of mammals, potentially by improving mitochondrial function or numbers, and trials of this nutritional supplement are underway.

Can we ever make new eggs? Living in the age of stem cell research, this idea appears to be moving from the realm of science fiction into the realm of possibility. We live in exciting times.



## About Atlantic Reproductive Medicine Specialists:



Founded by Dr. David Walmer and Dr. Susannah Copland, Atlantic Reproductive is a fertility clinic in Raleigh that blends a visionary approach to personalizing fertility care with the most advanced assisted reproductive technologies. Together we have more than 30 years of experience assisting patients in need through IVF, egg donation, sperm banking and more.



At Atlantic Reproductive, you will develop a one-on-one relationship with an approachable, board-certified reproductive endocrinologist. Together we will discover your fertility potential and tailor a treatment plan that is evidence-based and aligned with your personal values. You will then embark on your journey to parenthood with the reassurance that you will have access to the latest technologies, while working with a caring team dedicated to integrating the process into your life as seamlessly as possible.



Dr. David Walmer & Dr. Susannah Copland

