Reproductive Technologies, Inc.

THE SPERM BANK OF CALIFORNIA

2115 Milvia Street, Berkeley 94704 Phone 510.841.1858 Fax 510.841.0332 www.thespermbankofca.org

Conception Strategies for Women 35 and Older

The majority of TSBC recipients are age 35 and older, and nearly 60% of TSBC births in 2006-2007 were to women in this age range. While it is true that women over 35 face a particular set of challenges when trying to conceive, we know that these challenges can often be successfully overcome. This handout reviews some of the specific strategies available to women over 35 who wish to conceive a child.

The older you are, the less time you have to spend trying to conceive. While some women can conceive in their early 40's without medical intervention, the hard truth is that some women cannot conceive in their 40's even with assistance. For this reason, if you are over 35, we recommend that you have your fertility evaluated by a reproductive specialist. A fertility evaluation will give you valuable information that may impact the decisions you make in this process. You can expect your doctor to suggest some of the testing and fertility medications described below in the "Medical Strategies" section.

How Aging Affects Fertility

If you're healthy, fit, and still ovulate regularly, it may be hard to believe that you could experience road blocks on your path to pregnancy. Although being healthy and fit is important, the decline in fertility is a natural process that starts at least a decade before menopause begins. Women's fertility peaks when we are in our mid-20s and slowly declines after that.

Women are born with a finite number of egg follicles and as you age, so do the eggs that you've carried with you since you were a fetus yourself. And just as you have a higher chance of developing health problems as you grow older, so do your eggs. With age the egg follicles decline in quantity and quality-through ovulation and natural cellular death. We ovulate our healthiest follicles during our 20s and early 30s and by our mid-30s, both the health and number of remaining egg follicles (referred to as the "ovarian reserve") has diminished.

Successful fertilization of an egg and implantation of the resulting embryo involve an intricate series of hormonal feedback loops and a decline in the ovarian reserve has a significant effect on this process.

Pre-Ovulation Changes

In the days just prior to ovulation, the dominant egg follicle releases estrogen, which stimulates the production of fertile cervical mucus to help sperm on its journey through the cervix. An older egg follicle does not produce as much estrogen as a younger follicle which in turn means that not as much fertile cervical mucus will be produced.

Once enough estrogen has been produced, it will trigger a surge of luteinizing hormone (LH). This surge precedes ovulation by 12 to 48 hours. As we reach our mid-30s to early 40s, the LH surge is often lower than when we were younger and is sometimes too low to be detected by an ovulation predictor kit. Women over 35 may also notice that their fertile mucus may appear and disappear before the LH surge, whereas for younger women usually cervical mucus is most abundant during the LH surge.

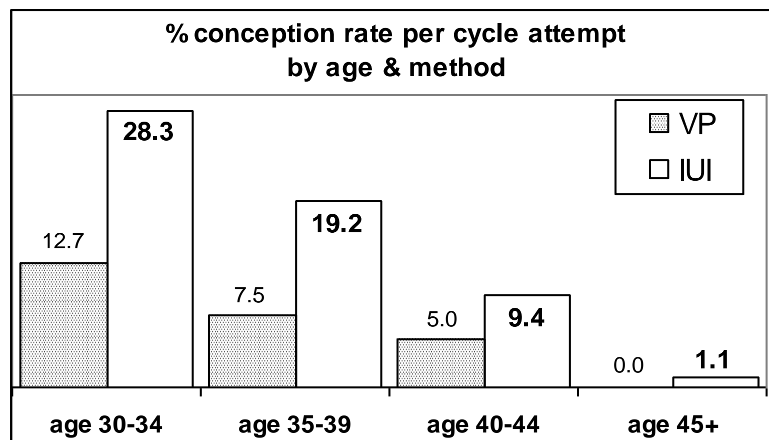
Post-Ovulation Changes
Once the egg is released into the fallopian tube, the collapsed follicle forms a structure called the corpus luteum, which produces progesterone, a hormone that creates a nourishing uterine environment for a fertilized egg. A corpus luteum resulting from a poorer quality egg follicle may not be able to produce enough progesterone for implantation to be viable. Furthermore, older eggs may divide abnormally early in embryonic life, so even if fertilization is successful, the probability of miscarriage increases with age.

Medical Strategies
Many of our recipients are reluctant to use fertility drugs or other interventions until they have tried a few natural cycles. This is understandable, and we encourage you to create an insemination plan that feels comfortable to you. However, it is helpful to have a plan of action in place before you start inseminating. In our "Make a Timeline" section below, we offer suggestions as to when you might want to seek medical assistance.

Intrauterine Insemination
Unless you have an abundance of fertile-quality cervical mucus that is correctly timed with your LH surge and other fertility indicators, we would urge you to choose intrauterine insemination (IUI) over vaginal insemination. The presence of cervical mucus is crucial for a successful vaginal insemination, but isn't necessary for a successful IUI. Furthermore, studies of insemination with frozen sperm have conclusively proven IUI to be twice as effective as vaginal insemination (e.g. see chart below).

TSBC Data

From 2004 through 2007, our overall conception rate per cycle attempt for IUI was 17.2% and for vaginal insemination was 8.5%. The chart at right shows the conception rate per cycle attempt by recipient age and insemination method.



Even though as women get older, the probability of conceiving decreases, IUI results in reasonable success rates for women in their early 40's, with women ages 40 - 44 on average experiencing a 1 in 10 probability of conceiving in any given cycle attempt. Note that this conception rate is similar to the success rates for women in this age group undergoing in vitro fertilization (IVF) using their own eggs.

Blood testing
The most common test used to evaluate fertility is known as the *Day 3* test. This simple blood test looks at the levels of Follicle Stimulating Hormone (FSH) and Estradiol (the type of estrogen produced by the ovaries) in your bloodstream on the third day of your cycle. If these levels are too high, it indicates that your endocrine system is working too hard to stimulate the development of egg follicles, and suggests a diminished ovarian reserve. High levels don't necessarily indicate that you can't conceive; but they do indicate that you may want to consider using fertility drugs to increase your chances of conception.

A progesterone level is another helpful test, generally done a week after ovulation. This level will indicate if you've ovulated effectively.

Clomid and Letrozole
Clomid (clomiphene citrate) is the most commonly prescribed fertility medication for women who are not ovulating or who ovulate immature follicles that don't produce enough progesterone for successful implantation. It is also sometimes used to cause *superovulation* (stimulating the hormones to produce more than one dominant egg follicle), with the goal of improving the chances of conceiving. Clomid works by suppressing the effects of estrogen, thereby tricking the body into producing more FSH.

Generally, it's not recommended that women take Clomid for more than four cycles, as conception rates plateau after three to four cycles. Some fertility providers may prescribe another drug that improves ovulation, Letrozole, instead of Clomid. Letrozole clears from the body more quickly than Clomid and sometimes works for women who do not respond to Clomid. It is a relatively new treatment and has similar effectiveness as Clomid. Women who conceive using Clomid or Letrozole have up to a 10% chance of conceiving twins.

A minority of women taking Clomid experience side effects, such as mood swings, hot flashes, headaches, and blurred vision. Also, some women find that these medications significantly change the length of their cycle and/or their fertility signs. If you experience any of these effects, we recommend you discuss them with your physician.

Progesterone
Women whose luteal phase (the second half of the cycle after ovulation) appears to be too short to sustain the uterine lining long enough for an egg to implant are often prescribed progesterone, either orally or in suppository form. However, it is generally more effective to improve your body's luteal phase progesterone by improving ovulation with Clomid or Letrozole.

Gonadotropins
Gonadotropins are naturally or synthetically derived versions of FSH and/or LH, which are injected to promote ovulation in women who either haven't had success using Clomid or who are preparing for an IVF cycle. These drugs stimulate the ovaries to produce multiple egg follicles, thereby increasing the chances of conception (and the chances of conceiving multiple embryos). They are powerful and expensive drugs, which are only prescribed when the woman's cycle will be closely monitored with regular ultrasounds of the ovaries to ensure that *ovarian hyperstimulation* syndrome doesn't occur. If pregnancy occurs, there is a 20-30% chance of conceiving multiple embryos. Some recent research studies question the value of Gonadotropin-stimulated IUI cycles and indicate that time to pregnancy and risk of multiples may be lower for women who go directly to IVF.

In Vitro Fertilization (IVF)
In vitro fertilization is a surgical procedure in which an egg (or eggs) is removed from a woman's ovary, fertilized with sperm, incubated in a laboratory, and the resulting embryo(s) placed in the woman's uterus. The Gonadotropin drugs discussed above are generally used to stimulate the ovaries prior to egg retrieval. IVF can be very successful for overcoming blocked fallopian tubes and other fertility issues, especially for women under 38. However, IVF does not improve egg quality and the success rate (defined as the live birth rate) is 6%-10% for women in their 40's using their own eggs. However, the success rate for women in their 40's using eggs donated by a younger woman, rises to greater than 40% per cycle.

Alternative Treatments for Fertility

Some women prefer to try alternative treatments for fertility before, in addition to, or instead of western medical treatments. Alternative treatments to increase fertility may include acupuncture and traditional Chinese medicine, Chinese herbs or other herbal supplements, mind-body programs, and special diet or exercise programs. There are fewer scientific studies on the outcome of these treatments and the studies that do exist are conflicted about whether there is any benefit. However, anecdotally, some TSBC recipients have reported success using non-western treatments as alternative or complementary methods to boost their fertility.

Make a timeline

While there are no hard and fast rules, we offer the following guidelines for maximizing your chances of conceiving.

- **We recommend all women consider having an honest preconception counseling session with a medical professional before trying to conceive.** Your provider may recommend doing some tests in preparation of your insemination attempts. Assessing your fertility early may increase your chance of success and decrease the time it takes you to conceive.

- **If you are between the ages of 35 and 40**, we encourage you to consult with a reproductive specialist after you have inseminated for three to six cycles without conceiving.

- **If you are between the ages of 40 and 42**, we advise you to consult with a reproductive specialist after two or three unsuccessful cycle attempts.

- **If you are between the ages of 43 and 44**, we highly recommend that you seek a reproductive specialist's advice before you begin the insemination process. Statistics suggest that by age 43, women have less than 10% chance of conceiving with their own eggs, 90% of which are chromosomally abnormal at this point. While it is not impossible to conceive and carry to term at this age, medical evaluation would help you avoid wasting valuable fertile time.

- **If you are 44 or older**, we strongly suggest that you consider using a donor egg, as the odds of successful conception with your own eggs are now very low. Of the over 2200 births reported to TSBC during the past 27 years, 4 (less that 0.2%) have been to women over 44 who conceived with their own eggs and all of these women conceived in the first 3 cycle attempts. Women's age-related decline in fertility is almost exclusively caused by aging in the egg follicles, not by aging of the uterus, so it is certainly possible to become pregnant and deliver a healthy baby with the help of an egg donor.

Emotional and Psychological Support

The process of inseminating can be stressful, additionally so for women with age-related fertility concerns. Each month can be a roller coaster of emotions. This stress can be further compounded for women who choose to keep their decision to inseminate private or who are taking fertility medications such as those discussed above. Many women find it helpful to actively seek out the emotional support of a few close friends, a support group, and/or a trained counselor. For women facing challenging conceptions, having caring, understanding people to talk to about your feelings and experiences becomes even more important. We encourage you to evaluate your support system and take steps to ensure that you have adequate emotional and psychological support throughout the insemination process.