Delaware Valley Institute of Fertility & Genetics
Conceptions
Spring 2003

What Defines Egg Quality?

By Kimberly Gleason, Ph.D.

A good quality egg clearly shows a pronounced zona (shell) and slightly grainy ooplasm.

Sometimes the shell of a poor quality egg is loose fitting and irregularly shaped.

A poor quality egg often has grainy, pockmarked ooplasm.

Many patients that plan to use in vitro fertilization (IVF) or another type of assisted reproductive technology know that egg quality is very important to achieving their goal of conceiving. What defines egg quality? A myriad of factors.

Physically, an egg is comprised of a shell (zona pellucida or "zona") and the cytoplasm (ooplasm) which, after fertilization, will grow into the cellular mass of the embryo. The function of the zona is to hold the ooplasm together, to regulate normal fertilization, to prevent abnormal fertilization such as polyspermy (fertilization by more than 1 sperm), and to protect the developing embryo from harm during its passage through the tubes and into the uterus.

Unlike the shells of bird eggs, our zonaes are thin, transparent, and slightly flexible, allowing us to visualize the embryo as it grows from a single cell to many cells during the first week of its life. The embryo will then escape or "hatch" out of its zona to prepare for implanting in the uterus.

In the laboratory, egg quality is assessed by thorough visual inspection. A good quality egg possesses a zona that is perfectly round without distortion, visually uniform in thickness, and precisely sized to encase the egg inside. A poor quality egg may have a zona that's too thick, which can hamper normal embryo hatching and implantation, or a zona that's too big for the ooplasm, which may allow the ooplasm to float around inside and become potentially damaged.

Surrounded by a thin membrane that helps to hold the egg together, the ooplasm also plays an important role in fertilization. It contains the nucleus of the egg (DNA) and many substances necessary for growth and development. A good quality egg has uniform color and its ooplasm is slightly granular. Its ooplasm also should be free of vacuoles (voids), or artifacts that appear as darkened dimples or nodules. Poor quality eggs may appear dark or degenerative, with focalized areas of intense granularity. They also may form ooplasm that has lost its consistency, becoming too watery or too firm.

What factors influence egg quality?

Many factors can influence the quality of eggs, which in turn, can influence a woman's chances of establishing a pregnancy. These factors include, but are not limited to: environmental, genetic, endocrine factors, and of course age. While there's not one single test that can be performed to determine egg quality inside the ovaries, the ultimate test of egg quality is the ability to become fertilized and subsequently to produce normal embryos and healthy babies.

Environmental

Exposure to radiation and X-rays has long been known to cause damage to the DNA of eggs. However, less obvious environmental factors can create problems within the ovaries that affect egg quality. For example, research in animals has demonstrated that exposure to extremes of temperature and humidity can lead to egg damage. Also, exposure to environmental pollutants such as organochlorides has been found to affect the normal growth cycle of eggs.

The environment within the ovaries is also very important in nurturing and supporting eggs. Inside of each follicle, or cystic area on the ovary, an egg may be growing and preparing itself for ovulation. The follicle is responsible for establishing and maintaining the appropriate ratios of the female hormones, primarily estrogen and progesterone, although many other hormones are involved. These hormones in turn provide a "micro" environment in the follicle that's critical for eggs to mature and grow properly. Any disturbances

Fast Fact:

A woman has the maximum number of potential eggs in her lifetime while still a fetus, at more than 7 million. It is estimated that by birth, this number has dropped to a little over a million, and by puberty is only about 300,000. Not all of these eggs will ever be ovulated.

in the normal hormone ratio within the microenvironment can negatively affect egg quality.

In addition, it is becoming more and more evident that lifestyle may indeed affect the eggs that are growing within the ovaries. For example, numerous reports over the past few years have demonstrated that smoking can affect the ability of an egg to become fertilized. This may explain why patients who smoke and undergo IVF generally have lower fertilization rates and therefore fewer embryos than do nonsmokers who undergo the same procedures. Although there has not been conclusive evidence to link smoking to poor egg quality, the ability of an egg to become fertilized is often a reflection of quality. The good news is that quitting smoking and making other healthy lifestyle changes prior to trying to conceive can restore good egg quality.

Genetic

It is quite routine in the laboratory to visually assess egg quality, although a "normal" appearing egg may possess underlying genetic defects. Likewise, an egg that appears "poor" may be chromosomally normal. Generally speaking, eggs with genetic flaws may often fail to fertilize, may fertilize abnormally, or may fail to develop normally. If our visual inspection fails to reveal any potential problems, nature has a way of correcting many defects on its own.

The most common genetic abnormality in eggs is failure to separate chromosomes evenly during growth. This defect of the egg can result in an entire embryo with an abnormal number of chromosomes, which results in a condition referred to as *"aneuploidy."* While it's impossible to predict whether or not an egg contains this condition via visual inspection, it is known that the incidence of aneuploidy increases with age. This may account, in part, for declining fertility in older women. Other genetic problems in eggs may result from failure of cytoplasmic components to properly control embryo cell division (growth).

Although there's no way to prevent genetic defects from occurring, new technology called preimplantation genetic diagnosis, in conjunction with IVF, can now allow us to test for chromosomal defects in an embryo. This breakthrough enables us to select and transfer only normal and healthy embryos back to the patient's uterus.

Endocrine

Just as the proper ratio of hormones within the follicle is critical for the normal growth of eggs, it's just as important to have normal overall levels of hormones circulating in the body. Because follicles and eggs can only respond to certain hormones during very precise intervals throughout the menstrual cycle, the various hormones are normally produced in different quantities depending on the day of the cycle. Premature exposure to the hormone LH, or exposure to high levels of androgens (male hormones) can affect eggs in the very early stages of growth inside the follicles. Patients with polycystic ovarian syndrome (PCOS) may produce higher than normal levels of testosterone, and typically produce numerous poor quality eggs through ART.

Proper diagnosis of the disease and control of hormones and metabolic processes with medications can increase chances of pregnancy by decreasing the damage to eggs.

Age

The fact that fertility declines with age is not news. However, new reports have suggested that fertility, due to egg factors, may begin to decline at age 27. This is much younger than previously thought. Although several other factors contribute to declining fertility, including diminished ovarian reserve, the most important factor is the declining quality of eggs. A recent report estimates that at age 42, 90 percent of a woman's eggs are genetically abnormal. Due to this fact and also the inability to over-stimulate the ovaries, ongoing pregnancy rates with IVF in women over the age of 40 using their own eggs remain under 15 percent.

There is obviously no way to turn back the hands of time, but new technologies are being researched that can possibly improve egg quality in older patients. In one of these highly experimental procedures, ooplasm from the eggs of young healthy women is injected into the eggs of older women. Researchers believe that the components of the ooplasm that control growth from the younger eggs are able to take over these responsibilities in the older eggs. The outcome is hopefully improved eggs that can continue on to fertilize and develop into healthy babies.

Another highly experimental procedure involves the replacement of the entire egg nucleus with that from young donor eggs. With this procedure, some of the chromosomal defects may be removed from unhealthy eggs.

Since these procedures are very invasive, experimental, and needless to say expensive, many older women opt to use eggs retrieved from young donors. The pregnancy successes in older women with donated eggs are very high, often over 70 percent!

An expert on in vitro fertilization (IVF) and embryology, Kimberly Gleason, Ph.D., is Delaware Valley Institute of Fertility & Genetics (DVIF&G) Director of Reproductive Laboratories. Dr. Gleason conducts pioneering research into factors affecting the outcome of various assisted reproductive technologies (ART). Her study results on evaluating sperm factors to optimize ART success will be published in the prestigious journal Fertility & Sterility this year. Her work has appeared in many other scientific journals. In 2003 she plans to study some of the factors affecting embryo quality and cryopreservation to help more patients conceive.

News You Can Use

LEAD EXPOSURE LINKED TO MALE INFERTILITY

A recent study published in the journal *Human Reproduction* found that lead exposure may cause some cases of unexplained male infertility by impairing sperm function. In a study of 140 couples that were trying to conceive via in vitro fertilization (IVF), the more lead a man had in his semen, the lesser the likelihood of his partner conceiving. Exposure to higher lead levels can cause problems with the sperm's ability to bind to the egg and also with its ability to fertilize the egg. Since none of the men studied were exposed to high levels of lead on the job, the researchers suggest that all men with unexplained infertility have their sperm tested for lead exposure. The study authors were able to lower lead sperm levels in participants by having them take zinc supplements. Men that want to conceive also should quit smoking and limit alcohol to one drink per day.

EASY EXERCISE

If you're trying to conceive or in the early stages of pregnancy, moderate exercise is best. A study conducted at the University of North Carolina at Chapel Hill found that moms-to-be who exercise at moderate intensity before pregnancy and during their first two trimesters have a reduced risk of premature delivery (a factor in infant mortality).

BREAST CANCER DRUG MAY HELP PATIENTS CONCEIVE

According to doctors at Cornell University in New York, the breast cancer drug tamoxifen may help cancer patients retain their fertility. In a study looking at the drug's effectiveness as a fertility drug, researchers found that it boosted egg production in a dozen breast cancer survivors. The new findings offer renewed hope for breast cancer patients who want to freeze embryos because they risk ovarian failure due to the toxic effects of chemotherapy. Although tamoxifen has been used as an ovarian stimulant, its use in IVF treatment has been neglected due to its success as a breast cancer therapy. The study is also notable because one of its participants gave birth to twins after taking tamoxifen to stimulate egg production. The results of the study were published in the journal *Human Reproduction*.

EXERCISE AND YOUR CYCLE

If you exercise vigorously for 30 minutes, five days a week, the length of time between your periods might increase by up to three days and affect when you're fertile. This increase occurs because regular workouts may influence hormones, according to a recent study conducted by scientists at Kaiser Permanente in Oakland, CA. To keep track of ovulation, you may want to consider using a basal body thermometer.

ANTIDEPRESSANTS AND PREGNANCY

Although taking selective serotonin reuptake inhibitors (SSRIs) while pregnant has been found to be safe for the fetus, a recent study published in the *American Journal of Psychiatry* suggests that SSRIs can raise the risk of premature birth by 5 percent. The study authors warn moms-to-be not to skip taking Prozac®, Zoloft®, or Paxil® if they truly need the medication. Maternal depression can also harm the fetus.

"Keep your face to the sunshine, and you cannot see the shadows."

— Helen Keller

DVIF&G
Delaware Valley Institute of Fertility & Genetics
Success Through Assisted Reproductive Technology START

6000 Sagemore Drive—Suite 6102
Marlton, NJ 08053

Conceptions

Conceptions is published quarterly for a select group of OB/GYNs and their patients. To receive extra copies of the newsletter or to be placed on our mailing list, please call Carla Scott at **(856) 988-0072** or e-mail her at: **info@startfertility.com.**

EDITOR: Christine Norris

DESIGN: JLDCreative/JLevins Design

Delaware Valley Institute of Fertility & Genetics
6000 Sagemore Drive—Suite 6102
Marlton, NJ 08053
(856) 988-0072

2791 South Delsea Drive
Vineland, NJ 08360
(856) 794-8080

3100 Princeton Pike
Bldg 4, Suite D
Lawrenceville, NJ 08648
(609) 895-0088

Visit our web site at:
www.startfertility.com

Happy Birthday to . . .

Stephanie Marie Forker, born on September 17, 2002, to Donna and Martin Forker

Daniel Leighton Bogart, born on September 20, 2002, to Lisa and David Bogart

Adam Douglas MacMillan, born on January 2, 2003, to Doug and Chivan MacMillan

Alaina Jones, born on January 22, 2003, to Heather and David Jones

Jacob Andrew Fritz, born on February 25, 2003, to Nancy and Andrew Fritz

Samantha True and Ryan True, born on March 18, 2003, to Randi and Randolph True.

All the babies and parents are doing well. Thank you, DVIF&G!

Ask the Doctors

Q: I'm 40 years old and due to the quality of my own eggs, I've been advised to use donor eggs to conceive a child with my husband via in vitro fertilization (IVF). But I'm a little nervous about using eggs from an anonymous donor. Can you help?

A: Since the quality of a woman's eggs declines as she ages, considering the use of donor eggs to conceive is another option. The pregnancy success rates for older women with donated eggs are very high, often over 70 percent, according to Kimberly Gleason, Ph.D., DVIF&G's Director of Reproductive Laboratories. Your concerns about using eggs from an anonymous donor are understandable. At DVIF&G, we don't have our patients use eggs from anonymous donors. Instead, we encourage patients to ask a family member or friend to donate their eggs to help them achieve their dream of having a baby.

We have found that by choosing a known donor, couples are more comfortable with the procedure. Some couples also choose to freeze donor embryos to try for another child at a later date. At our practice, patients can choose to store frozen embryos for up to five years. At that point they either have to use them or dispose of them.

Do you have a question for "Ask the Doctor?" Please e-mail your question to Christine Norris, *Conceptions* editor, at: christinenorris@earthlink.net For more "Ask the Doctors" questions and answers, visit our web site at: www.startfertility.com