Notable Grand Rounds
of the
Michael & Marian Ilitch
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FERTILITY AND FAMILY PLANNING IN RESIDENCY AND FELLOWSHIP

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About Notable Grand Rounds

These assembled papers are edited transcripts of didactic lectures given by mainly senior residents, but also some distinguished attending and guests, at the Grand Rounds of the Michael and Marian Ilitch Department of Surgery at the Wayne State University School of Medicine.

Every week, approximately 50 faculty attending surgeons and surgical residents meet to conduct postmortems on cases that did not go well. That “Mortality and Morbidity” conference is followed immediately by Grand Rounds.

This collection is not intended as a scholarly journal, but in a significant way it is a peer reviewed publication by virtue of the fact that every presentation is examined in great detail by those 50 or so surgeons.

It serves to honor the presenters for their effort, to potentially serve as first draft for an article for submission to a medical journal, to let residents and potential residents see the high standard achieved by their peers and expected of them, and by no means least, to contribute to better patient care.

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Fertility and Family Planning in Residency and Fellowship

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Grand Rounds presentation

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Introduction

Fertility and family planning are significant concerns for individuals pursuing medical careers, particularly those in residency and fellowship. With the intense demands of medical education and training, discussions around family planning are often delayed until later stages of life, when fertility challenges may arise. This paper aims to define key reproductive terms, explore age-related fertility decline, and discuss both female and male fertility, as well as provide an overview of fertility preservation options and in vitro fertilization (IVF). I discuss how career pressures, particularly in medicine, can impact family planning decisions and the potential consequences of delaying these decisions.

Defining Reproductive Terms

Before delving into the effects of age and career on fertility, it is essential to establish a common understanding of key reproductive terms. **Ovarian reserve** refers to the number and quality of eggs remaining in a woman's ovaries, which naturally declines with age. **Spermatogenesis** is the process by which sperm are produced in the male testes, which also declines in efficiency as men age. **Ovulation** is the release of a mature egg from the ovary, typically occurring once per menstrual cycle, and is necessary for fertilization. **Fertility preservation** involves medical interventions such as egg or sperm freezing, aimed at preserving reproductive potential for future use. Additionally, specific fertility challenges may involve terms like **primary ovarian insufficiency**, a condition where the ovaries stop functioning normally before age 40, leading to early menopause and infertility, and **azoospermia**, which refers to the absence of sperm in a man's semen, often caused by genetic, hormonal, or physical issues, making conception without medical intervention impossible.

Age-Related Fertility Decline

Fertility naturally declines with age, particularly for women, whose ovarian reserve diminishes with time. The most fertile years for women typically occur in their 20s, with a gradual decline beginning in the early 30s and a more significant decline after age 35. This phenomenon is often referred to as **age-related fertility decline** and is driven by both a reduction in the quantity and quality of oocytes (eggs). Male fertility, though more resilient to age, is not immune to decline, with sperm quality and motility decreasing with age, especially after the age of 40.

The Challenge of Timing in Medical Careers

One of the most common concerns among medical professionals is determining the "right" time to start a family. The typical trajectory of a medical career—undergraduate studies, medical school, residency, fellowship, and then establishing a practice—leaves little room for family planning. Young professionals often find themselves prioritizing career over personal life, only to reach their late 30s or early 40s and realize that starting a family may not be as simple as initially thought.

This delay in family planning is particularly common among medical professionals, who often focus intensely on their education and careers. However, the biological clock continues ticking, and by the time some individuals decide to start a family, fertility challenges may arise. It is not uncommon for professionals to find themselves sitting down at 35 or 39 thinking about starting a family, only to face tougher circumstances than they anticipated.

Fertility Misconceptions

Many individuals enter their childbearing years with misconceptions about fertility. Some believe that because family members conceived easily in their 40s, they too will have no issues. Others point to examples of older celebrities, such as Mick Jagger or Hugh Hefner, having children in their 70s and 80s, and assume that male fertility does not decline. Such misconceptions can lead to delayed family planning and unanticipated fertility struggles.

Every single patient I see wishes they had come in sooner. Many individuals do not realize how long conception can take, even under optimal conditions, or that factors such as irregular periods or untreated medical conditions can affect fertility. These challenges often become apparent only after a prolonged period of unsuccessful attempts to conceive, which could have been mitigated with earlier intervention or awareness.

The Impact of Birth Control and Fertility Expectations

Another common assumption is that discontinuing birth control will immediately result in pregnancy. Many women share the mindset that stopping birth control will open the floodgates and they will get pregnant instantly, but that's not always the case. For some, conception can take much longer than anticipated, especially if underlying fertility issues exist.

By the time many women discontinue birth control and begin trying to conceive, they may already be in their late 30s, when age-related fertility decline is more pronounced.

Early Awareness and Proactive Planning

Early awareness and proactive planning is very importaant when it comes to fertility. Medical professionals, in particular, may benefit from thinking about their long-term family goals earlier in their careers and making informed decisions about fertility preservation options.

Those considering having children in the future are encouraged to take steps toward family planning sooner rather than later. Just like they made plans to achieve their career goals, they should make plans for their personal goals, too.

During my OB-GYN residency, I found myself, like many of my peers, consumed by my professional responsibilities. At the age of 35, colleagues suggested I begin thinking about my own fertility, but like many in similar circumstances, I felt ill-prepared to act on this advice.

Ignoring Symptoms and Misunderstanding Risks

One of the key mistakes is a tendency to overlook subtle warning signs that may indicate underlying fertility issues. For instance, one resident dismissed her irregular periods, attributing them to a thyroid condition and the intense physical toll of residency. This sense of denial is not uncommon, particularly among individuals who are juggling the high-stress demands of medical training and practice. Fatigue, irregular menstruation, and other symptoms can be mistaken for mere consequences of a grueling lifestyle, when in fact, they may signal more serious reproductive health issues.

That particular resident's story took an unexpected turn when she experienced a miscar-

riage after finally conceiving. Following the miscarriage, she never had another period, leading to the discovery that she had entered **premature ovarian failure (POF)**, also known as **primary ovarian insufficiency (POI)**. Her experience illustrates the unpredictable nature of fertility, even for those who may not initially present with obvious risk factors.

Premature ovarian failure occurs when the ovaries stop functioning normally before the age of 40, resulting in diminished estrogen production and irregular or absent menstrual cycles. For that resident, this diagnosis meant that her only viable option for having a child was through the use of donor eggs. Reflecting on her journey, she told me it was the best thing she ever did, but many individuals too often assume that everything will work out without considering the potential hurdles.

Fecundability and the Inefficiency of Human Reproduction

In the broader context of fertility education, the inefficiency of human reproduction often surprises individuals who assume that pregnancy will happen quickly once they stop using contraception. **Fecundability**, or the probability of conceiving per menstrual cycle, decreases with each passing month. During the first two to three months of trying to conceive, the chance of pregnancy is approximately 30% per month. However, if conception does not occur within a year of regular, unprotected intercourse, the likelihood of conceiving drops to about 5% per month. By this point, medical professionals recommend seeking an evaluation, as 80% of couples will have conceived within that year.

Time is of the essence. As people delay family planning, especially those in high-pressure professions, the window of opportunity narrows. The recommendation for individuals over the age of 35 is to seek an evaluation after six months of trying, as age-related factors can impact both egg quality and the overall likelihood of conception. The decline in reproductive potential becomes more pronounced after age 35, and the ability to intervene early can make a substantial difference in the options available.

Misconceptions and Fertility Myths

Many individuals believe that once they stop using contraception, they will become pregnant immediately. This belief is rooted in the over-cautious use of contraceptives during one's 20s and early 30s, where avoiding pregnancy often feels like an ever-present risk. They stop birth control and feel like the floodgates are going to open, but in reality, human reproduction is not at all that efficient.

Additionally, there are myths surrounding male fertility and age. High-profile examples of older men, such as Mick Jagger or Hugh Hefner, fathering children well into their 70s and 80s contribute to the misconception that male fertility does not decline. However, while men can remain fertile into old age, sperm quality, motility, and the likelihood of successful conception diminish with time, particularly after age 40. These fertility myths can lead to a false sense of security, encouraging individuals to delay family planning only to discover that age-related factors complicate their ability to conceive.

The Reality of Infertility and Subfertility in Modern Medicine

The statistical reality is that approximately one in six couples will experience infertility, a number that has shifted from one in seven in recent years. This increase can be attributed to a variety of factors, including an aging population, environmental influences like microplastics, rising rates of obesity, and delayed family planning. While the underlying causes are multifactorial, the impact on individuals and couples is profound and the emotional toll is significant.

Basic Anatomy and Physiology of Reproduction

Understanding the anatomy and physiology involved in reproduction is fundamental to addressing the many variables that can affect fertility. The process begins with the ovaries, which contain all the eggs a woman will have in her lifetime. Each month, one egg is chosen to develop through a complex hormonal interplay involving **follicle-stimu-**

lating hormone (FSH) and **luteinizing hormone (LH)**. FSH acts as a "gas pedal," stimulating the growth of one follicle, which in turn produces **estradiol** (E2). Once estradiol reaches a certain threshold, it triggers a surge of LH, causing ovulation—the release of an egg from the ovary.

The egg is then captured by the **fimbriae** of the fallopian tube and moved toward the uterus by the action of tiny **cilia** lining the fallopian tubes. For conception to occur, sperm must travel through the female reproductive tract and fertilize the egg within the fallopian tube. The fertilized egg, now an embryo, makes its way to the uterus, where it (ideally) implants and begins to grow.

Causes of Subfertility and the Importance of a Proactive Approach

The term "subfertility" carries a more hopeful connotation than “infertility.” It implies that while conception may be challenging, it is not impossible. Subfertility can result from a variety of issues affecting either the male or female partner. For women, ovulatory dysfunction, diminished ovarian reserve, and blocked fallopian tubes are among the most common causes.

A blocked fallopian tube is particularly noteworthy because it can occur even in the presence of healthy eggs and sperm, rendering natural conception impossible. Conditions such as **endometriosis**, **pelvic inflammatory disease (PID)**, and **prior surgeries** are common contributors to tubal blockages. Endometriosis, in particular, has become increasingly recognized as a significant cause of subfertility. This inflammatory condition can cause scarring and adhesions around the fallopian tubes, creating barriers that prevent the egg and sperm from meeting.

Women who experience severe **dysmenorrhea** (painful periods), or **dyspareunia** (pain during intercourse) may be suffering from undiagnosed endometriosis. This condition can lead to **tubal occlusion**, where the tubes become so scarred that they are no longer pliable or functional.

Other potential causes of blocked fallopian tubes include infections such as **chlamydia**, an asymptomatic sexually transmitted disease that often goes undiagnosed and untreated. Chlamydia can cause significant damage to the reproductive tract, particularly the fallopian tubes. This is why routine testing for sexually transmitted infections is recommended for sexually active individuals, even in the absence of symptoms.

Structural Abnormalities and Their Role in Subfertility

Structural abnormalities of the uterus can also play a role in subfertility. **Fibroids**, **polyps**, and **congenital uterine anomalies** can all interfere with implantation or increase the risk of recurrent pregnancy loss. Fibroids, which are benign growths of the uterine muscle, may not always pose a problem. For instance, fibroids located on the outer surface of the uterus typically do not affect fertility. However, fibroids that protrude into the uterine cavity (**submucosal fibroids**) can disrupt the normal environment needed for embryo implantation and growth. These fibroids are also more likely to cause symptoms such as heavy menstrual bleeding or pain.

Similarly, congenital anomalies such as a **bicornuate uterus** (where the uterus has two distinct cavities) can make it more difficult to conceive and carry a pregnancy to term. Polyps, which are small growths of the uterine lining, can also develop over time and contribute to subfertility or recurrent miscarriages.

Evaluating and Addressing Subfertility

When a couple is unable to conceive after one year of regular, unprotected intercourse, a comprehensive fertility evaluation is recommended. This timeline is shortened to six months for women over the age of 35, as early detection and intervention are crucial for maximizing fertility outcomes. Approximately 80% of couples will conceive within one year of trying, with an additional 10% conceiving within the second year. However, for those who do not conceive within this window, fertility testing can identify issues such as tubal occlusion, ovulatory dysfunction, or male factor infertility.

The evaluation may include a **hysterosalpingogram (HSG)**, which uses dye and X-rays to assess whether the fallopian tubes are open, as well as blood tests to measure **ovarian reserve** and hormonal levels. Identifying and addressing underlying causes of subfertility—whether through medical treatment, surgery, or assisted reproductive technologies—can significantly improve the chances of achieving a successful pregnancy.

The Causes of Infertility and Diagnostic Testing

Infertility is a condition that can affect both men and women, with roughly 40% of cases attributable to female factors, another 40% due to male factors, and the remaining 20% resulting from a combination of both partners. The variety of causes leading to infertility necessitates a comprehensive approach to diagnosis and treatment, including assisted reproductive technologies like in vitro fertilization (IVF). Understanding the root cause of infertility is critical for determining the appropriate interventions, and this requires a thorough diagnostic workup.

Diagnostic Approaches to Female Fertility

For individuals or couples seeking to understand their fertility potential, a variety of diagnostic tests are available. One of the most common and straightforward tests is the **HSG** mentioned above, which evaluates the uterine cavity and fallopian tubes. During this procedure, a contrast dye is injected into the uterus, and X-rays or ultrasound imaging are used to observe the flow of the dye through the fallopian tubes. Ideally, the uterine cavity should have a triangular shape, and the dye should flow freely through both fallopian tubes. Any blockages or abnormalities, such as **unilateral tubal occlusion**, can be detected through this test.

Modern approaches to HSG are more comfortable for patients than in the past. Advances in ultrasound technology allow physicians to use **foam-based contrast agents** that eliminate the need for radiation and reduce discomfort. These methods also offer excellent resolution for visualizing the uterus and fallopian tubes, making them a valuable tool in fertility diagnostics.

Female Reproductive Potential and Ovarian Reserve

One of the most critical aspects of female fertility is **ovarian reserve**, or the quantity of eggs remaining in a woman's ovaries. Unlike men, who continuously produce sperm throughout their lives, women are born with all the eggs they will ever have. At 20 weeks gestation, a female fetus has approximately 6 million eggs, but by the time of birth, this number has already declined to around 1 million. By puberty, the number of eggs is reduced to approximately 300,000 to 400,000. From this point, the ovarian reserve continues to decline gradually, with a more pronounced loss beginning around age 35.

Because egg quantity diminishes over time, it becomes increasingly important to assess ovarian reserve, particularly for women in their mid-to-late 30s who are considering starting a family. There are several methods for measuring ovarian reserve:

1. **Anti-Müllerian Hormone (AMH)**: This hormone is produced by the small follicles in the ovaries. Higher levels of AMH indicate a greater number of remaining eggs, while lower levels suggest diminished ovarian reserve. An AMH level above 2 ng/mL is considered normal, while levels between 1 and 2 ng/mL indicate some diminished reserve. AMH levels below 1 ng/mL suggest more severe depletion of the ovarian reserve. The advantage of AMH testing is that it can be done at any point in the menstrual cycle and is not affected by contraceptive use.
2. **Follicle-Stimulating Hormone (FSH) and Estradiol Levels**: These hormones are measured on the second or third day of a woman's menstrual cycle. FSH, which stimulates the growth of ovarian follicles, increases as ovarian reserve declines. FSH levels below 10 mIU/mL are considered normal, while levels above 10 mIU/mL are suggestive of diminished ovarian reserve. However, this test must be interpreted alongside estradiol levels, as high estradiol levels can suppress FSH, leading to a falsely normal FSH result.

3. **Antral Follicle Count (AFC)**: During an **ultrasound**, the physician counts the small, immature follicles (typically less than 8 mm in size) visible in the ovaries. This provides an estimate of the number of eggs available for future ovulation cycles. A combined count of more than 10 antral follicles between both ovaries is considered normal. As ultrasound technology continues to improve, the threshold for what is considered a normal antral follicle count may increase, but the current benchmark remains a count of 10 or more.

Each of these methods offers valuable insights into a woman's ovarian reserve, and when used together, they provide a comprehensive picture of fertility potential. However, it is not uncommon for one measure to appear normal while another indicates a potential problem. For this reason, clinicians typically assess all three parameters to create the most accurate assessment.

The Importance of Timely Evaluation

As noted, the decline in ovarian reserve becomes more rapid after age 35. Women who are considering starting a family, or those who are unsure about their future family plans, should consider undergoing fertility testing to understand their reproductive potential. This proactive approach allows individuals to make informed decisions about their reproductive options, including whether to pursue fertility preservation techniques such as egg freezing.

Egg freezing, also known as **oocyte cryopreservation**, is an increasingly popular option for women who want to delay childbearing but are concerned about the natural decline in fertility with age. By freezing eggs during a period of higher fertility, women can preserve their reproductive potential for future use. This technology has advanced significantly in recent years, offering hope to individuals who are not yet ready to start a family but want to ensure they have options later in life.

Egg Quality and Its Impact on Fertility and Pregnancy

While egg quantity plays a critical role in a woman's fertility potential, **egg quality** is equally, if not more, important. Egg quality refers to the genetic health of the egg, which deteriorates as women age. A process known as **gametogenesis** (egg development) contributes to this decline.

Since women are born with all the eggs they will ever have, by the time of ovulation, these eggs have already undergone much of their maturation process. However, as a woman ages, the apparatus responsible for separating genetic material during cell division, called the **spindle apparatus**, can become less effective. The spindle apparatus is crucial during the final stages of egg development, as it ensures that chromosomes are evenly divided between the egg and a small polar body. This process, when functioning properly, results in a healthy egg containing the appropriate number (23) of chromosomes. However, with age, the spindle apparatus can become "sticky," leading to errors in chromosome separation. As a result, eggs can end up with too many or too few chromosomes, leading to **aneuploidies**, which are genetic abnormalities involving missing or extra chromosomes.

The majority of aneuploidies are **maternal in origin**, meaning they occur during the final stages of egg maturation before ovulation. This genetic instability becomes more pronounced as women age, which is why women over 35 are at greater risk for producing abnormal eggs.

The decrease in egg quality with age has profound implications for fertility. Even if a woman has a good **ovarian reserve**, the quality of the eggs she produces declines significantly after age 35. By age 45, more than 90% of a woman's eggs are likely to be genetically abnormal. This is why advanced maternal age is associated with both a decreased chance of conception and an increased risk of miscarriage.

Genetic abnormalities in eggs can also lead to **pregnancy loss**. The risk of carrying a genetically abnormal pregnancy increases with age. For example, by age 41, approximately 62% of pregnancies are abnormal, which most often results in miscarriage. This increased likelihood of miscarriage adds to

the challenges faced by women trying to conceive later in life.

Aneuploidies, such as **Down syndrome**, are well-known examples of genetic disorders resulting from abnormal egg quality. However, many aneuploid pregnancies result in early pregnancy loss, often before genetic testing or screening can be performed. This highlights the dual challenge of both achieving a pregnancy and maintaining a healthy pregnancy in women of advanced maternal age.

The "Fertility Clock" and the Importance of Early Action

Between the ages of 35 and 37, not only does it become harder to get pregnant, but the risk of miscarriage due to genetic abnormalities also rises significantly. By age 37, the chance of pregnancy and the likelihood of miscarriage are roughly equal, making it a pivotal point for women considering their family-building options.

Egg Freezing: Preserving Fertility for the Future

For women who are not ready to start a family but want to preserve their fertility, **egg freezing** offers a viable option. Egg freezing allows women to store their eggs at a younger age, when both egg quantity and quality are higher. The process involves daily injections of **FSH** (follicle-stimulating hormone) to stimulate the ovaries, followed by regular ultrasounds and blood tests to monitor the response. Once the eggs are mature, an **egg retrieval** procedure is performed under sedation, during which eggs are collected using a transvaginal ultrasound.

The retrieved eggs are then frozen and stored for future use. One of the key advantages of egg freezing is that the eggs retain the quality they had at the time of freezing. For example, a woman who freezes her eggs at age 25 and chooses to use them at age 50 will have the same chance of getting pregnant as she would have had at age 25. This effectively "stops the clock" on fertility, preserving the potential to have genetically healthy children later in life.

However, the success of egg freezing is closely tied to the woman's age at the time of freezing. Younger eggs are more likely to result in viable embryos and pregnancies. In contrast, freezing eggs at age 40, when approximately 90% of the eggs are genetically abnormal, requires a much larger number of eggs to achieve the same outcome as freezing eggs at age 25. Thus, women who are considering egg freezing are encouraged to act sooner rather than later, as the earlier eggs are frozen, the better the chances of achieving a healthy pregnancy in the future.

Considerations for Fertility Preservation and IVF

For couples who are in relationships and know they want to have children but are not ready to start a family, **fertility preservation** may be a viable option. For women who are unsure about their future partner or who have not yet decided who they want to have children with, **egg freezing** may be the best option. By freezing eggs, women preserve their fertility without needing to fertilize the eggs at the time of retrieval. This allows them to maintain control over their reproductive future without making decisions about parenthood with a specific partner.

However, for couples who are already committed to having children together but want to delay pregnancy due to career or other life circumstances, **embryo freezing** may be a better option. The process of embryo freezing is similar to egg freezing, with the main difference being that the eggs are fertilized with sperm after retrieval, and the resulting embryos are grown in the lab for five to six days before being frozen. This provides a "backup plan" for the future, ensuring that couples have healthy embryos available when they are ready to start a family.

A key advantage of embryo freezing is that the embryos can be genetically tested for **aneuploidy** (chromosomal abnormalities) before being frozen. This testing provides valuable information about the quality of the embryos, allowing couples to make informed decisions about which embryos to transfer when they are ready to pursue pregnancy. For example, a couple may retrieve four embryos, and after testing, find that three are genetically normal and one is abnormal. Knowing that they have three viable embryos

can offer peace of mind and flexibility for the future.

Costs and Insurance Coverage

Fertility preservation, whether through egg or embryo freezing, comes with significant financial considerations:

- **Medications**: The medications required for ovarian stimulation typically cost between $5,000 and $7,000. These medications are used to stimulate the ovaries to produce multiple eggs for retrieval, and the dosage needed may vary depending on the individual's age, weight, and ovarian reserve.
- **Procedures**: The process of egg retrieval and freezing also costs between $5,000 and $7,000. This includes the monitoring, ultrasound-guided retrieval, and freezing of the eggs or embryos.
- **Storage Fees**: Once the eggs or embryos are frozen, there is an annual storage fee of around $700 to maintain them in cryopreservation.

The total cost of fertility preservation can range from $10,000 to $15,000, depending on the individual's needs and response to treatment. For many, these costs can be prohibitive, especially without insurance coverage. While **IVF** is increasingly being covered by insurance plans, **egg freezing** for non-medical reasons (i.e., fertility preservation) is generally not covered. This is a significant gap in coverage that many hope will change over time as fertility preservation becomes more widely recognized as a valuable option for family planning.

Ethical Considerations of Egg Donation and Embryo Creation

For individuals or couples who choose to donate eggs, there are ethical implications that go beyond the immediate act of donation. Donors may wonder about the future of the children conceived from their eggs and grapple with the idea of genetic offspring they may never know.

The rise of **frozen egg banks** has made it easier for couples or individuals to access donor eggs when needed. For example, individuals can order a "six-pack" of eggs from a national egg bank and have them fertilized and transferred into the uterus. While this technology offers incredible opportunities for those who need donor eggs, it also raises questions about the long-term emotional and ethical consequences of having genetic children out in the world who may later seek out their biological parent(s).

Those considering egg donation or the creation of embryos are encouraged to reflect carefully on how they might feel about their decision in the future. The possibility of genetic linkage, the use of technology to track down donors, and the potential emotional impact of future connections between donors and offspring are all factors to consider.

In Vitro Fertilization (IVF): Expectations and Realities

In vitro fertilization (IVF) is one of the most powerful tools available in reproductive medicine, but it is essential to understand its capabilities and limitations.

The IVF Process: From Egg Retrieval to Blastocyst

IVF begins with ovarian stimulation. A woman undergoing IVF will take daily **FSH injections**, which stimulate the growth of multiple follicles in the ovaries. The goal is to produce a greater number of eggs than the body would naturally in a typical cycle, where only one egg matures. As these follicles grow, the ovaries are monitored closely through **ultrasounds** to determine when the eggs are mature and ready for retrieval.

Once the eggs are ready, the next step is the **transvaginal ultrasound-guided egg retrieval**. During this procedure, a needle is passed through the vaginal wall into the ovaries to suction out the fluid in the follicles, which contains the eggs. The retrieved follicular fluid are then handed over to the **embryologist**, who identifies eggs and either freezes the eggs or fertilizes them with sperm to create embryos.

If embryos are being created, a single sperm is injected into each egg through a procedure called **intracytoplasmic sperm injection (ICSI)**. This process significantly in-

creases the chances of successful fertilization, particularly in cases where male factor infertility is a concern. Once fertilized, the embryos begin to divide, progressing from two cells to four cells and eventually forming a **blastocyst**. The blastocyst stage, occurring five to six days after fertilization, offers the best chance of resulting in a successful pregnancy.

Genetic Testing of Embryos

At the blastocyst stage, some cells that are destined to become the **placenta** can be safely removed for genetic testing. This process allows the embryos to be tested for **aneuploidies** before they are frozen. This is crucial, especially for older women, as the risk of chromosomal abnormalities increases with age.

Testing helps identify which embryos are genetically normal and have the highest chance of resulting in a healthy pregnancy.

Advances in Egg and Embryo Freezing: Vitrification

The ability to freeze eggs and embryos has advanced significantly due to the process of **vitrification**, a rapid freezing technique. Eggs are especially challenging to freeze because they are the largest cells in the human body and contain a significant amount of water. In traditional freezing methods, ice crystals could form within the egg, damaging the fragile spindle apparatus responsible for proper chromosome separation.

With vitrification, eggs or embryos are placed in a small droplet of liquid and immersed into liquid nitrogen, freezing them so quickly that ice crystals do not have time to form. The result is a **glass-like structure** that preserves the integrity of the egg or embryo, allowing it to be stored indefinitely. There have even been cases where siblings are born decades apart from embryos created and frozen at the same time.

This technology has made it possible for eggs, embryos, and sperm to be safely shipped across distances. Frozen eggs or embryos can be transported with ease, making it possible for individuals to move or relocate without worrying about the geographic location of their stored reproductive material.

Setting Realistic Expectations for IVF

Despite its remarkable capabilities, IVF is not a guarantee of success. It is a tool that increases the number of eggs available for fertilization, but it cannot create more eggs than the ovaries are capable of producing. For example, if a woman has an **antral follicle count** of six, the maximum number of eggs that can be retrieved is six. Typically, about 80% of those eggs will fertilize, and around 40% will make it to the blastocyst stage.

The next important factor is the percentage of **genetically normal embryos**. For women under 35, approximately 50% of the embryos will be genetically normal. However, as women age, this percentage decreases. By age 40, nearly 90% of embryos are likely to be abnormal, meaning that more eggs and more egg retrieval cycles will be needed to achieve a similar number of viable embryos as in a younger woman.

It is also important to recognize that even with stimulation, some eggs may not develop into blastocysts. This can be emotionally challenging for individuals and couples, especially when multiple cycles of IVF are needed to achieve a viable pregnancy.

Costs of IVF and Insurance Coverage

IVF is a costly process, with **medications** alone ranging from $5,000 to $7,000 depending on the woman's age, ovarian reserve, and the dosage of hormones required. The **procedures** involved in IVF, including egg retrieval and embryo freezing, also cost between $5,000 and $7,000. Additionally, there are **annual storage fees** of approximately $700 for maintaining eggs or embryos in cryopreservation.

While IVF is increasingly being covered by insurance, **egg freezing** for non-medical reasons remains largely uncovered by insurance plans. This gap in coverage leaves many women and couples facing significant out-of-pocket expenses if they wish to preserve their fertility.

The Future of IVF and Fertility Preservation

Looking ahead, insurance coverage for IVF will likely continue to expand, particularly as public opinion around IVF evolves. However, the landscape of fertility preservation is still in flux, with egg freezing lagging behind in terms of insurance coverage. For now, those considering IVF or fertility preservation must carefully weigh the costs, benefits, and emotional impact of the process.

The Complexities of Egg Retrieval and Embryo Transfer in IVF

IVF is unpredictable. While the process follows a well-established protocol, the outcomes are far from guaranteed. The number of eggs retrieved, their quality, and the chances of successful fertilization depend largely on how an individual's ovaries respond to stimulation. Even with maximal doses of **FSH**, the response may vary, as ovaries sometimes don't respond as expected. This makes each cycle of IVF a delicate balance between treatment, experimentation, and testing to see how the ovaries will react.

How Many Eggs Are Enough?

One common question patients ask is, "How many eggs are enough?" Research suggests for someone age 35, retrieving **15 eggs** for the best chance of achieving multiple pregnancies. Specifically, 15 eggs offer:

- An 80% chance of having at least one child,
- A 40% chance of having two children, and
- A 10% chance of having three children.

However, even with this knowledge, there is no certainty that all follicles will respond to stimulation or that all retrieved eggs will be viable. The antral follicle count—a measure of the number of small follicles present in the ovaries at the beginning of a cycle—can give a good estimate of how many eggs might be retrieved. But ultimately, the ovaries' response to the medications is unpredictable.

Embryo Transfer: The Move Toward Singleton Pregnancies

One of the key goals in IVF today is to reduce the number of multiple pregnancies, which pose significant risks to both the mother and the children. Historically, transferring two or more embryos at a time was a common practice to increase the chances of pregnancy. However, current recommendations and guidelines favor **single embryo transfers (eSET)** to minimize the risk of twins and triplets.

At my clinic, we aim to transfer only one embryo at a time, regardless of the embryo's developmental stage (whether it is an early-stage embryo or a blastocyst). This approach aligns with guidelines from oversight bodies in reproductive medicine, which monitor clinics closely to ensure they adhere to best practices. Clinics that transfer more than one embryo routinely can face scrutiny, which may lead to negative repercussions, including more stringent monitoring and potential penalties.

While **fraternal twins** (non-identical twins) are more commonly associated with the use of medications like **Clomid** that stimulate the release of multiple eggs in a natural cycle, identical twins can still occur in IVF, even with single embryo transfers. There is about a 3% chance that a single embryo will split and form **identical twins**. The higher incidence of identical twins in IVF is thought to be related to how embryos are cultured in the lab, though the exact mechanisms are not fully understood.

Insurance, Financial and Logistical Considerations

In addition to medical guidelines, **insurance companies** play a significant role in regulating embryo transfer practices. Many insurance providers will not cover IVF procedures if more than one embryo is transferred at a time, further reinforcing the shift toward singleton pregnancies. While there is some frustration with insurance companies overall, their strict policies on embryo transfer have helped reduce the incidence of high-risk multiple pregnancies.

The cost of IVF has risen in recent years due to increases in the price of medications and supplies. These rising costs affect both clinics and patients, making fertility treatments less accessible for some individuals.

In summary, while IVF is a powerful tool for helping individuals and couples achieve pregnancy, it is important to approach it with realistic expectations. The number of eggs retrieved, the chances of successful fertilization, and the overall likelihood of a successful pregnancy depend on many factors, including age, ovarian reserve, and response to treatment. Additionally, current practices in IVF aim to minimize the risks associated with multiple pregnancies by transferring only one embryo at a time. Patients must also consider the financial and emotional costs associated with IVF and the evolving landscape of insurance coverage.

The Emotional and Physical Toll of IVF

IVF can be a deeply challenging process, both mentally and physically. Some patients undergo multiple **egg retrievals**—sometimes as many as 10 or 12 cycles—before achieving a successful pregnancy. While each cycle can increase the odds of success, the process can take a significant toll on patients' emotional and mental health. By the 10th retrieval, patients may start to experience symptoms of burnout and emotional fatigue. Even repetitive tasks, such as administering hormone injections, can become overwhelming, leading to feelings of confusion and exhaustion.

This emotional burden is compounded by the fact that each IVF cycle involves not only physical treatments but also significant emotional investment. Patients and couples must weigh the challenges of repeated cycles with the hope of eventually achieving their desired outcome. Individuals should consider their choices carefully, as the stress associated with IVF can be difficult to endure over time.

The Process of Embryo Transfer

Once an egg has been fertilized and becomes an embryo, the next step in IVF is **embryo transfer**. In this procedure, the embryo is placed into a **catheter**, which is then carefully inserted through the cervix and into the uterus under ultrasound guidance. The embryo is gently released into the uterus in the area that is most conducive to successful implantation. This process can be done with either a **fresh embryo** (immediately after fertilization) or a **frozen embryo**, which allows the body to recover from hormone stimulation before implantation. Freezing embryos also provides flexibility for individuals who may want to wait before attempting pregnancy.

For those who have frozen eggs, the process can occur when they are ready to create embryos, either with a partner's sperm or donor sperm, as needed. This flexibility allows individuals to pursue their reproductive goals on their own timeline.

Vitrification and the Numbers Game

Vitrification, which as noted prevents the formation of ice crystals within the cells, ensures that they remain intact and viable for future use. Vitrified reproductive cells can be stored indefinitely, providing patients with the security of knowing that their fertility is preserved.

However, IVF and fertility preservation are, to some extent, a **numbers game**. Not all eggs will mature, fertilize, or develop into viable embryos, and not all embryos will implant successfully. Nationally, it takes three embryo transfers to achieve one live birth. While some patients will conceive readily with a single embryo transfer, many will require multiple embryo transfers to achieve a live birth.

Male Fertility and the Role of Age

While much of the focus in IVF tends to be on female fertility, **male fertility** also declines with age, particularly after 35. **Leydig cells**, which produce testosterone, decrease by 50% between the ages of 20 and 48. This decline in testosterone affects **sperm count** and **sperm motility** (the ability of sperm to move efficiently), both of which are crucial for fertilization. By age 50, men may experience **andropause**, a period of low testosterone that can lead to symptoms such as fatigue, low libido, erectile dysfunction, and reduced sperm production.

One common misconception concerns the use of **testosterone supplements**. Some men seek testosterone treatments, but I strongly advise against this. Taking testosterone can suppress **FSH** and **LH**, the hormones responsible for stimulating sperm production, which can lead to **azoospermia**

(the absence of sperm in semen). Instead of improving fertility, these supplements can drastically reduce sperm production.

The Increasing Importance of Sperm Quality

Contrary to the old belief that sperm's only role was to fertilize the egg, new research shows that **sperm quality** is more critical than previously thought. Sperm not only contribute genetic material to the embryo but also play an important role in the development of a healthy pregnancy. As men age, the quality of their sperm decreases, including changes in **sperm morphology** (shape) and an increase in **DNA mutations** within sperm.

For every year a man is over 35, his sperm accrue **two new mutations**, and these genetic mutations can affect the quality of the embryo. This explains the increasing risk of genetic disorders, such as autism and schizophrenia, in children born to older fathers. The percentage of fathers over age 40 has grown in recent years, and this trend raises concerns about the potential impact on offspring health.

The Risks of Advanced Paternal Age

While men like Mick Jagger are often celebrated for fathering children at advanced ages, the reality is that **paternal age** has significant implications for reproductive success and offspring health. Studies show that older fathers are more likely to pass on genetic mutations to their children, increasing the risk of birth defects and other complications. As paternal age advances, the likelihood of pregnancy success decreases, and the risks associated with pregnancy and childbirth increase.

The Impact of Advanced Paternal Age on Fertility and Child Health

Paternal age is an often-overlooked factor in reproductive health. While much of the focus in fertility treatment is typically on maternal factors, research increasingly shows that the age of the father also plays a significant role in both pregnancy outcomes and the long-term health of children.

A retrospective study conducted by a urologist from Stanford University analyzed data from **40 million pregnancies** in the United States, using a CDC database. The researchers adjusted for **maternal age** (since aneuploidy is primarily maternal in origin) to isolate the effects of **paternal age** on pregnancy outcomes. Fathers over the age of 45 were associated with higher risks of adverse outcomes, including:

- **Low birth weight**,
- **Preterm delivery**,
- **Lower Apgar scores**, and
- **Seizures** in newborns.

In addition to these neonatal outcomes, the study found that advanced paternal age also had consequences for maternal health. Mothers carrying infants fathered by men over 45 had a higher risk of experiencing preterm birth complications, leading to hospitalization or procedures, and a greater likelihood of developing **gestational diabetes** compared to those with younger partners.

The Effect of Paternal Age on Sperm Quality

As men age, several key parameters of **sperm quality** begin to decline. These include:

- **Motility**: the ability of sperm to move efficiently toward the egg,
- **Morphology**: the size and shape of sperm, which affects their ability to fertilize an egg,
- **Fertilization capacity**, and
- **DNA integrity**.

The decline in sperm quality not only affects the chances of conception but also increases the risk of **adverse pregnancy outcomes** and health conditions in the child. Advanced paternal age has been linked to an increased risk of disorders such as:

- **Schizophrenia**,
- **Autism**,
- **Bipolar disorder**,
- **Childhood cancers** like leukemia, and
- **Klinefelter syndrome**, among others.

While there is no genetic test for complex conditions like **autism**, which are influenced by multiple factors, research has established

a clear association between older paternal age and a higher risk of these developmental and genetic conditions.

Monitoring Male Fertility: The Semen Analysis

For men concerned about their fertility, a **semen analysis** provides a simple and affordable way to evaluate sperm quality. The test, which costs around $150, assesses several key parameters, including:

- **Sperm volume**,
- **Total sperm number**,
- **Sperm concentration**,
- **Total motility** (whether the sperm are moving),
- **Progressive motility** (whether the sperm are moving efficiently toward the egg), and
- **Vitality** (the percentage of live sperm in the sample).

While many men may fall above the **lower reference limit** set by the World Health Organization (WHO), this threshold represents only the **5th percentile** of fertile men worldwide. Being at the 5th percentile is not ideal, and men should aim for higher-quality sperm to improve their chances of conception and reduce the risk of complications.

Various lifestyle factors can negatively impact **sperm DNA integrity** and increase the risk of **DNA fragmentation**, which is associated with **recurrent pregnancy loss**. Factors such as:

- **Diet**,
- **Stress**,
- **Infrequent ejaculation**,
- **High caffeine intake**, and
- **Exposure to environmental toxins** (e.g., in the workplace or operating room) can all contribute to sperm DNA damage.

For men experiencing recurrent pregnancy loss or other fertility issues, a **sperm DNA fragmentation assay** may be recommended, though it is not a standard test for most men. However, sperm freezing is an option for men who want to preserve their fertility. A sperm freeze typically costs around $300, and storage fees are less than $500 per year. Like frozen eggs and embryos, frozen sperm can be shipped across the country if needed.

Conclusion

I encourage both men and women to reflect on their reproductive goals and consider whether a fertility evaluation is appropriate. As with other major life investments—such as education and career—preserving fertility can be a valuable investment in one's future. If family building is a priority, taking proactive steps to preserve fertility may be worth the emotional, physical, and financial investment, especially in a landscape where insurance coverage for fertility preservation remains limited.

Fertility treatments like IVF and sperm freezing offer options for individuals and couples who want to delay family building or address fertility challenges. However, as I have emphasized throughout, it is crucial to make informed decisions based on personal goals, health factors, and realistic expectations about the outcomes of fertility preservation and assisted reproductive technologies.

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