NAME: EMIEJE AREROSUOGHENE PAUL

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EMBRYOLOGY ASSIGNMENT

OVULATION

Ovulation is the release of an egg from one of a woman's ovaries. After the egg is released, it travels down the fallopian tube, where fertilization by a sperm cell may occur.

Ovulation typically lasts one day and occurs in the middle of a woman's menstrual cycle, about two weeks before she expects to get her period. But the timing of the process varies for each woman, and it may even vary from month to month.

If a woman is hoping to become pregnant, she will want to keep track of when she may be ovulating. Knowing when a woman is ovulating each month is helpful because she is the most fertile — or able to become pregnant —around the time of ovulation.

A couple will be more likely to conceive if they have sex a day or two before a woman ovulates and the day of ovulation.

**Menstrual cycle and ovulation**

At birth, a female fetus has 1 to 2 million immature eggs called oocytes inside her ovaries, which is all the eggs she will ever produce. By the time a girl enters puberty, about 300,000 of these eggs remain. Approximately 300 to 400 of the remaining eggs will be ovulated during a woman's reproductive lifetime.

A likely sign that a woman is ovulating is that she is having regular, predictable periods that occur every 24 to 32 days.

With every monthly menstrual cycle, a woman's body prepares for a potential pregnancy. The cycle is regulated by hormones, including the sex hormones estrogen and progesterone, as well as follicle-stimulating hormone and luteinizing hormone. Hormones play a key role in all stages of the menstrual cycle, allowing the ovum (egg) to mature and eventually be released.

When a mature egg leaves a woman's ovary and travels into the fallopian tube, a sperm cell can fertilize the egg. Sperm can live inside a woman's reproductive tract for about 3 to 5 days after sexual intercourse, according to the Mayo Clinic. For pregnancy to take place, a sperm cell must fertilize the egg within 12 to 24 hours of ovulating, according to the Mayo Clinic. The fertilized egg then travels to the uterus, or womb, where it can attach to the lining of uterus and develop into a fetus.

During ovulation, the walls of the uterus also thicken to prepare for a fertilized egg. But if the egg is not fertilized, the uterine lining is shed about two weeks later, causing menstrual flow to begin. But simply having her period does not always indicate that a woman is ovulating.

"The most misunderstood thing about ovulation is the idea that if you are menstruating, it means that you are ovulating; and that is indeed not the case at all," said Dr. Mary Jane Minkin, a clinical professor of obstetrics, gynecology and reproductive sciences at the Yale School of Medicine.

Many women have an ovulatory cycle — the buildup of the lining of the uterus — because they are making estrogen. But when the buildup gets to a certain level, the lining just sloughs off, and a woman can bleed quite heavily. When a woman ovulates, she also makes the hormone progesterone, which results in a more controlled bleed.

**Timing / ovulation clues**

Many people mistakenly believe that ovulation always happens exactly 14 days after a woman's last period. But the timing of ovulation varies for each woman and depends on the length of her menstrual cycle.

If a woman typically has 28-day menstrual cycles, she usually ovulated between days 13 to 15; If her cycle ranges between 27 and 34 days, ovulation usually occurs between days 13 to 20.

Beside charting the timing on a calendar, a woman may have other clues that she could be ovulating. Her body may have one of the following three signs:

**1. Change in vaginal secretions.**

A few days before a woman ovulates, her cervix, which is the lower part of the uterus, produces a type of mucus that is thin, clear, slippery and stretchy. This change in cervical mucus occurs when ovulation is approaching and her ovaries are getting ready to release an egg. The day after ovulation occurs, cervical mucus undergoes another change and it becomes thicker and cloudy.

**2. Change in basal body temperature.**

Keeping track of a woman's basal body temperature, which is taken in the morning before she gets out of bed, for two to three menstrual cycles may help predict when she is fertile. Shortly after ovulating, many women show a slight increase (about 1 degree F) in early morning body temperature. A woman is most fertile during the 2 to 3 days before her temperature rises.

**3. Rise in luteinizing hormone.**

About 24 to 36 hours before a woman ovulates, her levels of luteinizing hormone increase. A rise in luteinizing hormone is a signal for the ovary to release an egg. This hormone increase can be detected by using an ovulation predictor kit, which can test a sample of urine in the days leading up to ovulation. When a rise in luteinizing hormones is detected, the test will show a positive result.

**Fertile window**

A woman is fertile — able to become pregnant — only during a certain part of her monthly cycle. The "fertile window" spans a 6-day period, the 5 days before ovulation and the day a woman ovulates. Studies suggest that intercourse is most likely to result in a pregnancy when it occurs in the three days leading up to and including the day of ovulation.

**Home ovulation test**

If a woman is getting her period on a monthly basis, but not getting pregnant, it may be because she is not ovulating. An ovulation predictor kit can be helpful to see whether a woman is, in fact, ovulating.

This kit, sold over-the-counter in drug stores, can test a woman's urine to detect if she is experiencing an increase in luteinizing hormone, which usually happens about 24 to 36 hours before ovulation occurs.

A woman may want to begin using the kit about 10 days after the start of her last period.

And if the test shows that ovulation isn't occurring, it's a great time to check in with your gynecologist: because getting women to ovulate is often quite straightforward. When ovulation is irregular or does not occur, doctors may try to induce the process by prescribing medication to stimulate a woman's ovaries to release an egg.

**Ovulation problems**

There are many reasons why a woman may have ovulation problems. Some women, for example, have blocked fallopian tubes due to pelvic inflammatory disease, endometriosis or surgery for an ectopic pregnancy.

An abnormal level of hormones can cause ovulation to be irregular or not occur at all, according to The American College of Obstetricians and Gynecologists. For example, polycystic ovary syndrome (PCOS), is a condition in which levels of certain hormones are abnormal and a woman does not get her period or it is irregular. Thyroid problems can also make the ovaries less likely to release an egg.

A woman who is underweight with a body mass index (BMI) of 18.5 or less may have irregular menstrual cycles and it could also cause ovulation to stop, according to the American Society for Reproductive Medicine. At the opposite end of the weight spectrum, obesity may also lead to irregular periods and irregular ovulation.

In addition, the timing of ovulation can be affected by factors, such as stress and excessive exercise. Emotional or physical stress may delay ovulation or prevent a woman from ovulating. Getting too much intense physical activity can also inhibit ovulation.

DIFFERENCES BETWEEN MEOISIS 1 AND MEOISIS 2

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| MEOISIS 1 | MEOISIS 2 |
| Heterotypic division | Homotypic division |
| Reduces the chromosome number in the daughter cell | Equalizes the chromosome number of both parent and daughter cells |
| Homologous chromosomes are present at the beginning | Individual, bivalent chromosomes are present at the beginning |
| Chromosomal cross-over occurs during prophase 1 | No chromosomal cross-over occurs during prophase 2 |
| Preceded by interphase | No interphase takes place |
| A complex division and takes more time | Comparatively less simple and takes less time |
| Individual chromosomes are present in the daughter nuclei | Sister chromosomes are present in the daughter nuclei |
| Prophase 1, metaphase 1, anaphase 1 and telophase 1 are the four phases | Prophase 2, metaphase 2, anaphase 2 and telophase 2 are the four phases |

STAGES INVOLVED IN FERTERLIZATION

Stage 1. Preparation of the Sperm

Ejaculated sperm are not ready to fertilize an egg when they enter the vagina. In response to the dilution of semen in the vagina, they undergo several changes, which are collectively known as capacitation

1.Intracellular Ca++ levels increase.

2.Spermatic motility is activated and tails change beat frequency.

3.Sperm cell surface antigens are lost. The loss of these proteins renders the sperm more receptive to binding to the egg.

Stage 2. Sperm-Egg Binding

Because of the availability of gametes, the process of sperm-egg binding was first studied and understood in invertebrates . In sea urchins, the sperm head binds directly to the egg outer surface and this triggers the acrosome reaction. The acrosomal contents are released and there is a balanced Na+ influx and H+ efflux, causing an increase in pH. The increased pH triggers the dissociation of the profilactin complex (actin and profilin) and the released actin monomers polymerize to form a filament called the acrosomal process. This acrosomal process penetrates the egg coatings to allow fusion of the sperm and egg plasma membranes. In sea urchins then, the sperm literally skewers the egg. In humans the process of sperm-egg binding is not so simple. The complicating factor is the thick zona pellucida, which keeps sperm from binding close to the egg plasma membrane.

Sperm receptor on egg

Dr. Paul Wassarman used a competition assay to isolate and identify the factor in the zona pellucida that was involved in sperm egg binding . Dr. Wassarman incubated sperm with zona pellucida glycoproteins (ZPGPs) he had isolated from unfertilized and fertilized eggs. He found that sperm preincubated with ZPGPs from unfertilized eggs were not able to fertilize eggs. Yet, when he preincubated sperm with ZPGPs isolated from fertilized eggs, which are known not to bind sperm, the sperm could still fertilize eggs. This showed that the isolated ZPGPs from unfertilized eggs contain a receptor for the sperm and that this receptor is modified after fertilization. In follow up experiments, Dr. Wassarman purified ZPGP I, ZPGP II and ZPGP III and showed that only ZPGP III could prevent sperm binding to eggs showing that ZPGP III is the sperm receptor. By treating ZPGP III with agents that selectively hydrolyzed protein (trypsin), N-linked glycoproteins (specific glycohydrolase) and O-linked glycoproteins (weak base), Dr. Wassarman showed that the part of ZPGP III that was responsible for sperm binding was the O-linked oligosaccharide.

Egg receptor on sperm.

What sperm component is binding to the ZPGP III? Dr. Barry Shur was studying a Golgi enzyme known as galactosyl transferase. This enzyme catalyzes the addition of galactosyl residues from a donor nucleotide sugar, UDP-galactose, to the terminal end of O-linked oligosaccharides. As in all enzymatic reactions, there are two stages in catalysis:

1.The enzyme binds the substrates (in this case UDP-gal and O-linked oligosaccharide).

2.The enzyme catalyzes the reaction and releases the products (in this case, UDP and the modified Olinked oligosaccharide with galacosyl residues on its ends).

It is important to understand that if one of the substrates is not present, the enzyme may be able to bind the available substrate, but will not be able to catalyze the reaction. This is important in sperm binding. Dr. Shur found that sperm, which have no Golgi apparatus, have galactosyl transferase on the surface of their plasma membrane. When sperm are ejaculated, they have oligosaccharides bound to the galactosyl transferase. During capacitation, these coating glycoproteins are removed, allowing the galactosyl transferase, to bind to other carbohydrates it may encounter, such as those attached to ZPGP III. The sperm that do encounter the egg and its zona pellucida, bind ZPGP III through their galactosyl transferases. At this point, UDP-gal would normally bind to its site on galactosyl transferase, galactose residue would be transferred to the oligosaccharide and the modified oligosaccharide would be released. However, there is no high energy UDP-galactose in the extracellular fluid surrounding the egg so catalysis does not occur and the sperm remains tightly bound to the egg zona pellucida. Many studies support a role for galactosyl transferase as the sperm protein involved in sperm-egg binding, however, other proteins may be involved. A recent genetic knockout of galactosyl transferase in mice yielded mice that were completely fertile and showed normal sperm-egg binding.

Acrosome reaction.

As a result of irreversible binding of the sperm to the egg, the zona pellucida triggers the acrosome reaction. The outer plasma membrane of the acrosome fuses at multiple sites with the plasma membrane and the contents of the acrosome are released. Two of the important components are acrosin, a serine protease, and N-acetylglucoaminidase. Acrosin bores a hole in the zona pellucida so that the sperm can reach the egg itself. N-acetylglucoaminidase hydrolyzes the O-linked oligosaccharides in ZPGP III to allow the sperm to detach. As a result of the membrane fusion, a new surface is exposed on the sperm (the inner acrosomal membrane) and this is thought to contain new binding sites for ZPGP II.

Stage 3.Sperm-Egg Fusion

For many years the process by which the plasma membrane of the sperm and egg fused was a black box. Recent studies by Drs. Judith White, Diana Miles, and Paul Primakoff and their colleagues, have now shed light on this process. Miles and Primakoff made an antibody to PH-30, a heterodimeric sperm membrane protein comprised of α and β subunits, and showed that this antibody blocked fertilization but did not block binding of sperm to eggs stripped of their zona pellucida. This suggested that PH-30 was involved in sperm and egg fusion and it was given the name fertilin. Cloning and sequencing of fertilin revealed that the αsubunit had a hydrophobic domain that resembled those on viral proteins that are known to be involved in membrane fusion. The β-subunit had a disintegrin domain. Disintegrins were first discovered in snake venom and act as competing ligands for integrins (for example, snake venom disintegrins will block platelet aggregation mediated by integrins). Both subunits had metalloprotease domains. Fertilin was one of the first proteins of a family of proteins known as ADAMs proteins (for A Disintegrin And Metalloprotease containing protein) that are involved in cell-cell recognition and cell fusion events. Although the mechanism for how fertilin causes sperm-egg membrane fusion is not known, studies have supported its role in membrane fusion. For example, a peptide corresponding to the viral fusion peptide of α-fertilin is capable of fusing model membrane vesicles and the disintegrin domain of β-fertilin will block sperm-egg fusion. The egg integrin involved in sperm-egg fusion (the receptor for the β-subunit disintegrin) is known to be α6β1. Once the sperm fuses with the egg, the beating of the tail stops immediately. The sperm instead is drawn into the egg by elongation and fusion of the egg’s microvilli. As a result, the sperm nucleus and other organelles are incorporated into the egg cytoplasm. The sperm nucleus undergoes a series of changes, including chromatin decondensation and formation of a new nuclear envelope, to form a male pronucleus. The male pronucleus uses microtubules to migrate to the center of the cell, where it fuses with the female pronucleus to reconstitute a diploid nucleus. Other sperm organelles (e.g., mitochondria) persist during early cleavage stages of the embryo and it is conjectured that they may play a role in development.

Stage 4. Activation - The Egg’s Response

The immediate events after fertilization include the egg’s effort to prevent polyspermy. Polyspermy refers to the fertilization of the egg by more than one sperm, resulting in zygotes with greater than a diploid amount of DNA. This causes early embryonic defects and arrest of development. After sperm-egg fusion, the egg mounts the cortical reaction to prevent polyspermy. In all eggs, residing just under the plasma membrane there are membrane bound vesicles known as cortical granules. When a single sperm penetrates the egg, the cortical granules adjacent to the site are triggered to fuse with the plasma membrane, exocytosing their contents into the perivitelline space (the space between the plasma membrane and the zona pellucida). The cortical reaction is propagated over the surface of the egg by a wave of Ca++ . This was shown by the aequorin experiment in which the photoprotein aequorin phosphoresced in a wave from the site of sperm penetration of the egg 1-10 As a result of the cortical reaction, two important enzymes are released into the perivitelline space:

1. Ovoperoxidase: In sea urchins, ovoperoxidase catalyzes the crosslinking of tyrosine residues in the extracellular matrix. This makes the extracellular matrix tough and insoluble (analogous to the tanning of leather) and a physical barrier is formed which prevents other sperm from fertilizing the egg. In mammals, ovoperoxidase does not catalyze tyrosine cross-linking to the point of insolubility. In mammals, its major effect is thought to be as a spermicial agent.
2. Hydrolase. Remember Wassarman’s result showing that zona pellucida from fertilized eggs was incapable of blocking fertilization? Another cortical granule that is released is a specific hydrolase, which degrades O-linked oligosaccharides on ZPGP III. This renders the zona pellucida incapable of binding additional sperm, thus preventing polyspermy.

Activation of the egg also includes the initiation of development of the new zygote. Protein synthesis and other metabolic processes are upregulated to provide for the developing embryo.

DIFFERENCES BETWEEN MONOZYGOTIC TWINS AND DIZYGOTIC TWINS

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| MONOZYGOTIC TWINS | DIZYGOTIC TWINS |
| They are developed by the splitting of a fertilized embryo into two | They are developed by separate fertilizations of two eggs by two sperms |
| Cause is not known | Caused either by IVF, certain fertility drugs or hereditary predisposition |
| Genetic codes are nearly identical | Genetic codes are same as any other sibling |
| Gender is the same | Gender is different |
| Blood types are the same | Blood types are different |
| Appearance is extremely similar but may be affected by environmental factors | Appearance is similar as any other siblings |
| One-third of the twins in the world are monozygotic | Two-thirds of the twins in the world are dizygotic |
| Can be either Di-Di, Mono-Di or Mono-Mono twins | Only Di-Di twins |