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Human Biology

Human Reproduction, Fertilization and Pregnancy
Discussion Questions

The events at the ovum at the moment of fertilization are an intricately organized series of biochemical events designed to attract any sperm but to allow only one sperm to enter into the egg. Describe some key events of this process and how more than one sperm is prevented from entering the egg? Why is preventing more than one sperm in so important?

When sperm nears an egg, it travels through the corona radiata, an extracellular matrix on the egg's surface. This part reminds me of docking a ship and several sperm can actually make their way into the corona radiata "docking station" at one time. The next phase, breaking through the zona pellucida, the egg's outer membrane, is not as easy. The point of the sperm binds to a receptor in the zona pellucida and the acrosome at the sperm's tip releases digestive enzymes. In this way, the sperm digests itself a path into the cytoplasm of the egg. The pronuclei of the sperm and egg then fuse, which creates a zygote. If more than one sperm were allowed to break through into the cytoplasm, things would get awfully tricky in the chromosome department. Since a sperm and an egg contain only 23 chromosomes apiece, they are designed to fuse at a 1:1 ratio to achieve the magic number of 46 chromosomes. Allowing the nuclei of additional sperm to penetrate the zona pellucida could result in the creation of "zygotes" with far too many chromosomes (I am assuming these rogue creations would commit apoptosis or perhaps be dealt with by immune cells, rather than developing at all. Nevertheless, if multiple sperm were allowed into the egg at once, it would make human reproduction much more challenging because pregnancy would only result in the instances when the pronuclei of just a single egg and sperm joined to achieve 46 chromosomes). Fortunately, an egg contains protections to insure that only a single sperm has the chance to move past the zona pellucida. When the first sperm makes contact with the egg, the egg's plasma membrane immediately depolarizes which prevents any other sperm from binding to it. The next step involves secretion of enzymes by cortical granules in the egg. These harden the zona pellucida so that the egg becomes impenetrable (the exterior is now called the fertilization membrane). Thus, the new zygote is protected from the addition of extra genetic information from more sperm. It is truly a "winner takes all" process in which the first sperm on the scene has the chance to create a zygote while its "competitors" are effectively frozen out by the egg.

What is the role of progesterone in pregnancy? How does the location of making progesterone change during the course of a pregnancy? What do you think would happen if all progesterone production was suddenly 'shut off' in a pregnancy?

Presence of progesterone in pregnancy signals the hypothalamus and anterior pituitary gland to prevent new follicles from beginning in the ovary and, consequently, additional eggs from being released. Put simply, this insures that woman cannot develop a secondary pregnancy weeks or months after fertilization and essentially places the ovarian cycle on pause until the pregnancy has ended. Progesterone also maintains the uterine lining for the embryo and relaxes smooth muscles. This allows the uterus to expand with the growing fetus and also expands the arteries. Expansion of arteries decreases the blood pressure and begins the renin-angiotensin-aldosterone mechanism which is aided by estrogen and ultimately responsible for a significant increase in blood volume during pregnancy. Although the relaxation of smooth muscles during pregnancy plays a vital role in making room for the baby and insuring an adequate blood supply for mother and fetus, it also causes some of the unpleasant side effects associated with pregnancy, including heartburn (caused by relaxation of the esophageal sphincter) and constipation (due to decreased contraction of intestinal walls).

Prior to ovulation, progesterone is produced in a secondary follicle in the ovaries. Once an egg has been released, LH is secreted from the pituitary gland which causes the corpus luteum to develop and release a significant amount of progesterone. This makes sense because of the role progesterone plays in thickening the uterine lining--in essence, its volume increases to create a more hospitable environment for implementation of the zygote. The corpus luteum is responsible for secreting progesterone at the beginning of pregnancy but eventually the placenta takes over this role (presumably once it has had time to mature). When the placenta can produce progesterone in sufficient quantities to support the pregnancy, the corpus luteum becomes unnecessary and is said to “regress” (I don’t quite understand if that term simply means decompose or if there is something more complicated occurring).

It would be extremely dangerous if progesterone production failed during pregnancy. First, it is a decrease in progesterone that signals the uterus to shed its lining in menstruation. If the uterus receives the cue to shed the lining, an immature zygote could easily be effectively carried away by the process of menstruation. Later in pregnancy the placenta would be badly damaged, leaving the fetus unable to receive maternal blood. Secondly, I doubt it would be possible to maintain a pregnancy if progesterone-inspired muscle relaxation did not occur--the uterus would lack the necessary flexibility to make space as the fetus grew and blood supply would be insufficient to support the life of both the mother and child. I find hormones fairly confusing (why does it always seem that one releases another before they cause things to happen?) but progesterone clearly plays a critical role in maintaining a safe pregnancy and allowing a zygote to grow to viability as a healthy baby.

How do birth control pills work? What hormonal state women can have do the birth control pills imitate?

Birth control pills work by using estrogen and progesterone to stop production of FSH and LH--they essentially jump the gun on the negative feedback loop of the ovarian cycle. Without

the presence of these two hormones, an ovarian follicle does not develop and release an egg. Thus, women taking birth control pills do not ovulate. Ironically, the elevated levels of estrogen and progesterone essentially trick a woman's body into believing it is already pregnant and should not release another egg. There are several different formulations of birth control pills, some that involve taking hormones actively for three weeks, then taking a week off (or taking an inactive pill to maintain the daily habit); other birth control pills involve taking three months' worth of active hormones. Even while taking birth control pills, some amount of lining builds up in a woman's uterus and is released through menstruation during the phase of taking inactive pills, whether that be once a month or only 3-4 times a year.

Given all that hormones do in our body, I actually find it somewhat surprising that birth control pills work as well as they do! If the estrogen and progesterone in a birth control pills successfully signals the brain not to release FSH and LH, do they not also cause a very thick endometrium or begin mimicking what happens during pregnancy? In other words, how can birth control pills trick the pituitary gland and essentially signal that pregnancy has occurred without unleashing a cascade of other pregnancy-related events? Perhaps I am thinking too far beyond simply the ovarian cycle here but it seems to me that the dosing of synthetic estrogen and progesterone would need to be extremely precise to avoid confusing a woman's body mightily!

Why are the first three months of pregnancy the most dangerous for developing birth defects? When is the common age of the pregnancy when pregnancy tests become positive?

During first three months of pregnancy, which include the pre-embryonic and embryonic stages, all the major organs and body systems begin to develop. The first two weeks involve implantation and formation of the embryonic disk and primary germ layers through gastrulation. This effectively "sets the stage" for embryonic development. As early as the third week in pregnancy, the nervous system is established. Development of the heart also begins around this time. The umbilical cord becomes fully formed around the fourth week, allowing the embryo to receive sufficient quantities of maternal blood and ridding itself of waste. Limbs also develop in the first trimester and, at the beginning of the fetal development phase three months into pregnancy, the fetus is recognizably human. Needless to say, the transition from a zygote moments after fertilization into a miniature (though incomplete) human after three months is truly astounding. It also emphasizes the vulnerability of an embryo during the early months because critical body systems are established then. If a mother does not eat enough nutritious food during this stage it can have a serious impact on development. For example, lack of folic acid in the first trimester can lead to neural tube defects such as spina bifida and anencephaly. Use of alcohol, tobacco, or other drugs can have harmful effects at any time during pregnancy but it is logical to presume that these substances cause the most damage during critical early development rather than at the "fine tuning" that occurs later in pregnancy. As the mind-bogglingly complex development of human life occurs, it is perhaps helpful to see the process as a precise chronology where events must unfold in a certain order because one sets the stage for the next. Unlike cooking, say, where a forgotten ingredient may be thrown in at the

end, an embryo cannot simply delay or “do-over” early development, so any damage in the first months of pregnancy can have a permanent effect.

One of the interesting, highly-precise early events of pregnancy is when it can be registered affirmatively by a test. Implantation typically occurs six days after fertilization. At that time, the chorion secretes chorionic gonadotropin (hCG) which signals the corpus luteum to remain intact and continue to produce progesterone. The progesterone inhibits menstruation by maintaining the endometrium, which is critical to the developing embryo (estrogen is also secreted by the corpus luteum until the placenta is sufficiently established to make both hormones). About two days after implantation, on day 8 of the official pregnancy, sufficient hCG hormone would be present in a blood test to confirm pregnancy, which is quite remarkable precision in a nine month process!

Is the diaphragm, used by itself without spermicide, a barrier method of birth control? Explain why or why not. Can it prevent passage of STDs?

If one were to base birth control decisions on google searches--which is a terrible idea!--the diaphragm repeatedly appears listed as a barrier method of contraception. The diaphragm is a latex cup that is intended to fit over the cervix to prevent sperm from entering the uterus. However, a woman needs to follow directions carefully and insert the diaphragm perfectly in order to truly create a barrier (in addition, spermicide is highly recommended which does not inspire confidence in the diaphragm’s’ ability to maintain a barrier!) Given that a diaphragm cannot create a truly tight seal at the cervix, the term “barrier method” should probably be viewed as an overstatement (perhaps “barrier attempt” would be more precise). This is speculation on my part, but I imagine that a diaphragm could potentially be displaced during sexual intercurse because it does not include an exterior “anchor” in the way that a female condom does. Given the enormous volume of sperm released during ejaculation and their small size, there is certainly risk of sperm getting through a diaphragm’s “barrier.” In fact, failure rates hover between 18-20% for typical users. It’s interesting to note that the diaphragm has just a 5% failure rate for “correct and consistent use” (http://americanpregnancy.org/preventing-pregnancy/diaphragm). The statistical difference in failure rates is noteworthy--although it may be hard to ascertain how many women fall into the “typical” category, a one in five chance of pregnancy with misuse should give women pause, especially if they consider pregnancy avoidance highly important.

Diaphragms are not an effective way to prevent sexually transmitted diseases because viruses and bacteria need not enter a woman’s uterus in order to spread. Since the diaphragm just attempts to block the cervix, disease can still spread in the vagina. For example, chlamydia typically affects the lower regions of the reproductive tract (although the infection can be much more severe if it reaches the uterine tubes and can cause pelvic inflammatory disease).