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NURSING

Vaginal Insemination

The complex process of sperm transport through the female reproductive tract begins at the time of ejaculation. During coitus, 1.5- to 5.0-ml of semen containing between 200 and 500 million sperm is deposited at the posterior vaginal fornix, leaving the external cervical os partially submerged in this pool of fluid.[1] At this time, some sperm may be passively taken up by the cervix in a process described as “rapid transport;” otherwise, sperm undergo “delayed transport.” Both of these are discussed at length in this chapter.

The optimal pH for sperm viability is between 7.0 and 8.5,and a reduction in sperm motility is seen at a pH less than 6.0.Normal vaginal pH is only 3.5 to 4.0,and the acidic environment of the vagina is thus toxic to sperm. However, both seminal fluid and cervical mucus present within the posterior vagina are alkaline and act as buffers. Fox and coworkers have shown that vaginal pH rises to 7.0 within just seconds after ejaculation, and this decrease in acidity can be maintained for up to two hours after ejaculation.

Within about 1 minute after coitus, the ejaculate undergoes coagulation. This coagulum temporarily restricts movement of sperm out of the seminal clot, thus preventing their passage into the cervical mucus and ascension up the female reproductive tract. Over the next 20 to 30 minutes, however, a seminal-fluid proteolytic enzyme produced by the prostate gland gradually liquefies the clot. At this time, motile sperm may then enter the cervical mucus, leaving behind the seminal plasma. Although there are reports of motile sperm persisting within the vagina for up to 12 hours after ejaculation,motility of most vaginal sperm is diminished within about 30 minutes, and after 2 hours almost all sperm motility in the vagina has been lost.

Rapid Sperm Transport

Sperm may begin to undergo the process of rapid sperm transport within seconds after ejaculation. This type of sperm movement is thought to be predominantly passive, resulting from coordinated vaginal, cervical, and uterine contractions. Although these contractions are of short duration, they are believed to be the primary force responsible for the rapid progression of sperm to the upper female reproductive tract—the oviduct. Settlage and coworkers in 1973 reported results of a study in which fertile ovulatory females were intravaginally inseminated with donor sperm at the time of bilateral salpingectomy for sterilization. Within 5 minutes after insemination, sperm were present within the Fallopian tubes, and the number of sperm found there was proportional to the number inseminated.Similar results demonstrating this rapid transport process have also been documented in numerous animal studies.

The Cervix

Several important functions have been attributed to the cervix, and these include

- Providing a receptive environment for sperm entry near the time of ovulation
- Preventing access of sperm, microorganisms, and particulate matter to the upper reproductive tract and thus, the peritoneal cavity
- Filtering spermatozoa and removal of seminal plasma
- Preventing sperm phagocytosis by white blood cells within the female reproductive tract
- Providing a biochemical environment sufficient for sperm storage, capacitation, and migration

The structure of the human cervix facilitates performance of the these stated functions. The endocervical canal has an average length of 3.0 cm, and it is lined by two types of columnar epithelial cells, ciliated and nonciliated. The cervix does not contain true glandular units; rather, the mucosa is arranged with a series of infoldings that form crypts off the central canal. The nonciliated columnar epithelial cells secrete mucin granules, and the ciliated cells propel the cervical mucus from the crypt of origination toward the external cervicalos. Production of mucus is perhaps the most important function of the cervix, and this is discussed at length later in the chapter. Finally, cervical pH is alkaline, with a peak pH during the periovulatory period. This environment is much more hospitable to spermatozoa than the acidic pH of the vagina.

Cervical Mucus

Cervical mucus is continuously secreted through exocytosis by the nonciliated epithelial cells that line the cervical canal. This biomaterial serves many important functions, including exclusion of seminal plasma, exclusion of morphologically abnormal sperm, and support of viable sperm for subsequent migration to the uterus and oviduct. It is a heterogeneous fluid with both high- and low-viscosity components. The amount of mucus produced and its composition and characteristics fluctuate with circulating progesterone and estrogen levels. As estrogen levels peak at midcycle, cervical mucus is abundant in volume and thin in consistency because of increased water content. Under the influence of progesterone, water content decreases, and the mucus has a much higher viscosity.

Ultrastructurally, cervical mucus can be seen as a complex biphasic fluid with high viscosity and low viscosity components. The high viscosity gel phase is composed of a network of filamentous glycoproteins called *mucin*.Collectively, mucin macromolecules form a complex of interconnected micelles, which comprise a lattice whose interstices are capable of supporting the low viscosity phase, which is predominantly water. Sperm movement through the cervical mucus is primarily through the interstitial spaces between the mucin micelles, and the sperm's progression depends on the size of these spaces.The size of the interstices is usually smaller than the size of the sperm heads; thus, sperm must push their way through the mucus as they proceed through the lower female genital tract.

Besides hormonal factors, physical processes, such as shearing, stretching, and compression can alter the spaces between molecules and, consequently, orientation of the mucin filaments. These mechanical forces can be imparted by thrusting and pelvic contraction during coitus, and also by cervical contractions in the pericoital period. Additionally, rheologic forces associated with the mucus outflow from the cervical crypts tend to align the mucin filaments in a longitudinal fashion within the cervical canal, thus creating aqueous channels between the filaments. Given this longitudinal orientation, with mucus outflow originating in the crypts of the cervical epithelium, it has been postulated that sperm are constrained to swim in the direction of least resistance, that is, along the tracts of mucus outflow in the direction of the cervical crypts. Using mucus stretched *in vitro,* several investigators have indeed demonstrated the parallel swimming patterns of sperm. This theory complements the notion that spermatozoa entering the cervix are directed toward the cervical crypts, the site of mucus secretion that serves as a possible storage reservoir. Spermatozoa may retain their fertilizing capacity in human cervical mucus for up to 48 hours and their motility for as long as 120 hours. From their temporary storage location within the cervical crypts, sperm can be released gradually over time, thus enhancing the probability of fertilization.

Another potentially important feature of human cervical mucus is the belief that it is able to restrict migration of human spermatozoa with abnormal morphology. The percentage of spermatozoa with normal morphology in the cervical mucus and in the uterine fluid is significantly higher than usually seen in semen.

Quantitatively, these findings have been demonstrated following artificial insemination in which the percentage of sperm with normal morphology from the inseminated specimen was known ahead of time, thus allowing a more accurate comparison of the postinseminate semen within the cervical mucus.These results suggest that spermatozoa with abnormal morphology may be constrained by a process of restricted entry into cervical mucus. Comparison of morphologically normal versus abnormal human sperm in semen has shown that abnormal sperm are less likely to be motile, and those that are motile tend to swim with a lower velocity than normal cells. Katz and colleagues studied human sperm motility and morphology *in vitro* and they found that sperm with normal morphology swim faster than sperm with abnormal morphology, despite similar flagellar frequencies and amplitudes. These results suggest that morphologically abnormal spermatozoa may experience decreased movement resulting from increased resistance of mucus.

Sperm Transport Through the Uterus

Little is known about sperm transport within the endometrial cavity. Sperm motility does not appear to be the only force directing the sperm toward the oviducts, because inert particles deposited within the uterus are transported to the Fallopian tubes. Uterine muscular contractions likely play a role in this process. Unfortunately, much difficulty has been met in attempts to recover and quantify uterine sperm. Moyer and colleagues examined sperm recovered at the time of ovulation from the uterus of women undergoing hysterectomies 25 to 41 hours after intercourse. Sperm was recovered in only 6 of 26 women, and for these women the total number of sperm ranged from 1 to 4. None of the sperm were motile.

A study by Kunz and coworkers used vaginal sonography to demonstrate that uterine peristalsis during the follicular phase of the menstrual cycle exhibits an increasing frequency and intensity of subendometrial and myometrial peristaltic waves as the follicular phase progresses. During this portion of the cycle, the number of contractions propagating in the fundocervical direction decreased, and number of contractions progressing in the cervicofundal direction increased. In another part of this same study, the investigators placed technetium-labeled albumin macrospheres, about the size of spermatozoa, into the posterior vaginal fornix. The ascension of these particles was monitored by serial scintigrams. As soon as 1 minute after placement, the macrospheres reached the intramural and isthmic portion of the oviduct. Quantitatively, the number of macrospheres progressed dramatically as the follicular phase progressed, with only a few particles entering the uterine cavity during the early follicular phase of the menstrual cycle. By the midfollicular phase, the proportion of macrospheres entering the uterine cavity increased dramatically, and by the late follicular phase, the highest level of macrosphere transported to the oviducts was noted. Perhaps the most striking finding of this particular study was the preferential transport of these inert particles to the oviduct ipsilateral to the side of the dominant follicle. Other investigators have shown that near the time of ovulation, the number of spermatozoa is higher in the oviduct ipsilateral to the dominant follicle than in the contralateral oviduct on the side of the nondominant follicle. Several responsible forces have been proposed, including chemotaxis of the sperm toward the dominant follicle. The results of the above study, however, seem to suggest that lateralizing muscular contractile forces may play a significant role in this preferential movement, in that inert particles are obviously unable to engage in chemotactic migration.

Fallopian Tube

The adult human Fallopian tube, about 9 to 11 cm long, consists of five distinct segments: the fimbria, infundibulum, ampulla, isthmus, and intramural segment. The epithelial lining of the tube is composed of four cell types: ciliated, secretory, intercalary (peg), and undifferentiated cells. Epithelial cells undergo histologic changes in response to cyclic estrogen and progesterone variations, with the height of the epithelial cells being greatest at the time of the estrogen peak near midcycle. Tubal musculature is organized in a spiral fashion, and at the tubouterine junction these muscles become continuous with the myometrium.

Sperm movement through the Fallopian tube relies on a combination of forces: intrinsic sperm motility, tubular muscular contraction, and fluid flow. Tubal fluid production is maximal at the time of ovulation, and this fluid sustains the sperm before fertilization. Tubal fluid may also facilitate both sperm capacitation and acrosomal reaction.

Although the uterotubal junction does not act as a barrier to inert particles, it may serve as an additional functional barrier to sperm with abnormal morphology or motility. The number of sperm that reach the oviduct is many orders of magnitude lower than the total number of sperm in the ejaculate. Although tens of millions to hundreds of millions of sperm are deposited in the vagina at the time of ejaculation, anatomic studies have shown that typically only hundreds of sperm are present in the oviduct at various postcoital timepoints. Williams and colleagues studied the number and distribution of spermatozoa within the human oviduct near the time of ovulation. Parous women undergoing total abdominal hysterectomies for menorrhagia were inseminated with partner or donor semen, and 18 hours later, during surgery, both oviducts were ligated into ampullary, isthmic, and intramural regions. Using flushing techniques, scanning electron microscopy, and homogenization procedures, patients' oviducts were carefully evaluated for the presence of sperm. A median of only 251 total sperm was recovered from the oviducts of these women, and the ampulla near the ovulating ovary contained a significantly higher percentage of spermatozoa than did the nonovulatory side.

The precise role played by tubal fluid in gamete transport and sperm activation is still not entirely understood. Zhu and colleagues used an *in vitro* technique to demonstrate that human oviductal fluid maintains sperm motility induced by exposure to follicular fluid longer than does exposure to a simple salt solution. Furthermore, these investigators reported that the sperm acrosome reaction, which is induced by follicular fluid, is modulated by exposure of spermatozoa to tubal fluid. These findings may suggest that tubal fluid potentiates the motility and viability of spermatozoa, thus enhancing the chances of fertilization. Yao and colleagues used *in vitro* oviductal cell cultures incubated with spermatozoa to determine that oviductal cells promote capacitation and stabilize the acrosome. There is still much to learn about the dynamics of spermatozoa and the tubal environment. Although done in an *in vitro* setting, new studies such as the ones already discussed will likely provide clarity to the complex interplay between male gametes and the female reproductive tract.