

NAME-AFABOR MARIAN OGHENERUME

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QUESTION-Discuss the Factors Facilitating the Movement of Sperm in the Female Reproductive Tract

At coitus, human sperm are deposited into the anterior vagina, where, to avoid vaginal acid and immune responses, they quickly contact cervical mucus and enter the cervix. Cervical mucus filters out sperm with poor morphology and motility and as such only a minority of ejaculated sperm actually enter the cervix. In the uterus, muscular contractions may enhance passage of sperm through the uterine cavity. A few thousand sperm swim through the uterotubal junctions to reach the Fallopian tubes (uterine tubes, oviducts) where sperm are stored in a reservoir, or at least maintained in a fertile state, by interacting with endosalpingeal (oviduct) epithelium. As the time of ovulation approaches, sperm become capacitated and hyper activated, which enables them to proceed towards the tubal ampulla. Sperm may be guided to the oocyte by a combination of thermo taxis and chemo taxis. Motility hyper activation assists sperm in penetrating mucus in the tubes and the cumulus oophorus and zona pellucida of the oocyte, so that they may finally fuse with the oocyte plasma membrane. Knowledge of the biology of sperm transport can inspire improvements in artificial insemination, IVF, the diagnosis of infertility and the development of contraceptives. Passage of sperm through the female reproductive tract is regulated to maximize the chance of fertilization and ensure that sperm with normal morphology and vigorous motility will be the ones to succeed.

Oocytes are usually fertilized within hours of ovulation. On the other hand, in some species, sperm may be inseminated days (horses, cattle and pigs) or even months (some bat species) before the arrival of the oocyte. In humans, there is evidence that fertilization occurs when intercourse takes place up to five days before ovulation. Because sperm are terminally differentiated cells, deprived of an active transcription and translation apparatus, they must survive in the female without benefit of reparative mechanisms available to many other cells. Sperm are subjected to physical stresses during ejaculation and contractions of the female tract, and they may sustain oxidative damage. Furthermore, because sperm are allogeneic to the female, they may encounter the defenses of the female immune system meant for infectious organisms. Thus, sperm must somehow use their limited resources to maintain their fertility in the face of numerous impediments. As it is, of the millions of sperm inseminated at coitus in humans, only a few thousand reach the Fallopian tubes and, ordinarily, only a single sperm fertilizes an oocyte.

Vaginal defenses against infectious organisms may affect sperm

The vagina is open to the exterior and thus to infection, especially at the time of coitus; therefore, it is well equipped with antimicrobial defenses. These defenses include acidic pH and immunological responses and can damage sperm as well as infectious organisms. To enable fertilization to take place, both the female and the male have adopted mechanisms for protecting sperm. In humans, semen is deposited at the external of the cervix so that sperm can quickly move out of the vagina. Human sperm must contend, however briefly, with the acidic pH of vaginal fluid. The vaginal pH of women is normally five or lower, which is microbicidal for many sexually transmitted disease pathogens. Evidence indicates that the acidity is maintained through lactic acid production by anaerobic lactobacilli that feed on glycogen present in shed vaginal epithelial cells. Lowering pH with lactic acid has been demonstrated to immobilize bull sperm. The pH of seminal plasma ranges from 6.7 to 7.4 in common domestic species and has the potential to neutralize vaginal acid. Vaginal pH was measured by radio-telemetry in a fertile human couple during coitus. The pH rose from 4.3 to 7.2 within 8 s of the arrival of semen; whereas, no change was detected when the partner used a condom. Vaginal washings of women with high levels of detectable seminal antigens had a median pH of 6.1, whereas the median pH of washings lacking detectable antigens was 3.7. Contraceptive gel designed to maintain a low vaginal pH after coitus has been shown to immobilize human sperm *in vitro* and *in vivo*. In addition to pH buffers, seminal plasma contains inhibitors of immune responses, including protective components that coat sperm. These are most effective when sperm are bathing in seminal plasma and may be gradually shed when sperm leave the seminal plasma behind.

Males may also overcome female defenses by inseminating many sperm. This strategy is particularly effective for overcoming cellular immune responses. In the rabbit, deposition of semen results in an invasion of neutrophils into the vagina. This invasion takes time, however, to build to an effective level. Numerous leukocytes, many containing ingested sperm, were recovered from vaginas of rabbits 3–24 h post coitus. By that time, however, thousands of sperm had already reached the Fallopian tube.

Sperm transport through the cervix

In some species, the cervical canal widens under the influence of estrogen. Fluoroscopy and scintigraphy have been used in domestic dogs and cats to examine cervical patency. Opening of the cervix in these species has been correlated with estrus. Radiopaque fluid and also human serum albumin radiolabelled with technetium 99 could be seen rapidly passing through the cervix and filling the uterine lumen after deposition in the cranial vagina at estrus.

Sperm of humans and cattle enter the cervical canal rapidly where they encounter cervical mucus. Under the influence of estrogen the cervix secretes highly hydrated mucus, often exceeding 96% water in women. The extent of hydration is correlated with penetrability to sperm. Coitus on the day of maximal mucus hydration in women is more closely correlated with incidence of pregnancy than coitus timed with respect to ovulation detected using basal body temperature.

Cervical mucus presents a greater barrier to abnormal sperm that cannot swim properly or that present a poor hydrodynamic profile than it does to morphologically normal, vigorously motile sperm and is thus thought as one means of sperm selection. The greatest barrier to sperm penetration of cervical mucus is at its border, because here the mucus microarchitecture is more compact. Components of seminal plasma may assist sperm in penetrating the mucus border. More human sperm were found to enter cervical mucus in vitro when an inseminate was diluted 1:1 with whole seminal plasma than when it was diluted with Tyrode's medium, even though the sperm swam faster in the medium. Like the vagina, the cervix can mount immune responses. In rabbits and humans, vaginal insemination stimulates the migration of leukocytes, particularly neutrophils and macrophages, into the cervix as well as into the vagina. Neutrophils migrate readily through midcycle human cervical mucus. In rabbits, neutrophils were found to heavily infiltrate cervixes within an h of mating or artificial insemination. Interestingly, it was discovered that if female rabbits were mated to a second male during the neutrophil infiltration induced by an earlier mating, sperm from the second male were still able to fertilize. Thus, although the cervix is capable of mounting a leukocyte response, and neutrophils may migrate into cervical mucus, the leukocytes may not present a significant barrier to sperm. It has been demonstrated that neutrophils will bind to human sperm and ingest them only if serum that contains both serological complement and complement-fixing anti-sperm antibodies is present. This can happen in vivo if the female somehow becomes immunized against sperm antigens. Altogether, the evidence indicates that leukocyte invasion serves to protect against microbes that accompany sperm and does not normally present a barrier to normal motile sperm, at least not shortly after coitus. immunoglobulin's, IgG and IgA, have been detected in human cervical mucus. Secretory IgA is produced locally by plasma cells in sub epithelial connective tissue. The amount secreted increases in the follicular phase but then decreases at about the time of ovulation. The immunoglobulins provide greater protection from microbes at the time when the cervical mucus is highly hydrated and offers the least resistance to penetration. However, when there are antibodies present that recognize antigens on the surface of ejaculated sperm, infertility can result.

Complement proteins are

Sperm may also be guided through the cervix by the microarchitecture of the cervical mucus. Mucins, the chief glycoproteins comprising cervical mucus, are long, flexible linear molecules (molecular weight of human mucins is approximately 107 Daltons). The viscosity of mucus is due to the large size of mucins, while elasticity results from the entanglement of the molecules. It is thought that these long molecules become aligned by the secretory flow in mucosal grooves and thus serve to guide sperm. Human sperm have been demonstrated to orient themselves along the long axis of threads of bovine cervical mucus. Human sperm swimming through cervical mucus swim in a straighter path than they do in seminal plasma or medium.