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Discuss the factors facilitating the movement of sperm in the female reproductive tract

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 allogenic 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.

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. Radioopaque 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.

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 cervices within a h of mating or artificial insemination. Interestingly, it was discovered that if female rabbits were mated to a second male during the neutrophilic 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 leukocytic 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 leukocytic 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.

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. 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 and bull 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.

Are sperm stored in the cervix?

Little is known about how long sperm spend traversing the cervix or whether sperm are stored there. Vigorously motile sperm have been recovered from the human cervix up to 5 days after insemination, and the presence of sperm in mid-cycle cervical mucus forms the basis of the ‘post coital test’. Nevertheless, it is not known whether sperm collected from cervices this long after coitus would reach the Fallopian tube and succeed in fertilizing, nor could it be known whether these sperm had re-entered the cervix from the uterus. Very few sperm have been recovered from human uteri 24 h after coitus and those sperm are greatly outnumbered by leukocytes. Unless sperm are protected from phagocytosis (and they appear to be), it is unlikely that they could travel from a cervical reservoir to the oviduct 24 h post coitus.

Sperm transport through the uterus

At only a few centimetres in length, the human uterine cavity is relatively small and could be traversed in less than 10 min by sperm swimming at about 5 mm/min, which is the swimming speed of sperm in aqueous medium. The actual rate of passage of human sperm through the uterus is difficult to determine due to experimental limitations. Variation is high among women within a study and between studies. In one set of experiments, fertile women were inseminated into the cranial vagina shortly before surgical excision of both Fallopian tubes. Sperm were recovered from the fimbrial segment of the ampulla in two women whose tubes were removed 5 min after insemination, even though they had been abstinent for at least 16 days. Sperm were recovered all along the tubes of two more women merely 10 min after insemination. Unfortunately, the motility of these sperm was not assessed; therefore, it could not be determined whether the sperm were capable of fertilizing. In another study, several motile sperm were recovered from Fallopian tubes following hysterectomy 30 min after insemination in one patient and 1 h after insemination in three out of seven patients; however, these women underwent surgery for treatment of fibroids, polyps or endometriosis and therefore sperm transport may have been abnormal.Transport of sperm through the uterus is likely aided by pro-ovarian contractions of the myometrium. Ultrasonography of the human uterus has revealed cranially directed waves of uterine smooth muscle contractions that increase in intensity during the late follicular phase. The uterine contractions occurring in women during the periovulatory period are limited to the layer of myometrium directly beneath the endometrium. This is in contrast to contractions occurring during menses, which involve all layers of the myometrium. In cows and ewes, electromyography has indicated that strong contractile activity occurs during estrus, while contractions are weak and localized during the luteal phase.

Studies of uterine contractions during estrus should be interpreted with caution if coitus did not occur. Video-laparoscopic examination of mated and unmated rats revealed significant changes in contractile patterns of the uterine horns after mating. Unexpectedly, the change consisted of several-fold increases in both cranially and caudally propagating circular contractions. Caudally directed peristalsis would be expected to carry sperm away from the uterotubal junction. In estrous domestic cats, both ascending and descending contractions were observed by fluoroscopy. Perhaps the ebb and flow of contractions direct fresh waves of sperm to the uterotubal junction.

Myometrial contractions may be stimulated by seminal components. When vasectomized male rats were mated with females, the incidence of strong uterine contractions declined, indicating that sperm or testicular or epididymal secretions have stimulatory activity. Removal of the seminal vesicles significantly reduced the pregnancy rate in mice. In boars, there is evidence that estrogens, which may reach 11.5 μg in an ejaculate, increase myometrial contraction frequency. Since boar semen is deposited directly into the uterine cavity, the uterus is exposed to the full amount of estrogens in the semen. There is evidence that the estrogens enhance contraction by stimulating secretion.

When sperm first enter the uterus, they outnumber the leukocytes. As time passes, the leukocytes begin to outnumber the sperm. Also, as sperm lose protective seminal plasma coating, they may become more susceptible to leukocytic attack. At some point, even undamaged sperm may fall victim to the leukocytes. Probably, to ensure fertilization, sperm should pass through the uterine cavity before significant numbers of leukocytes arrive.

Transport through the uterotubal junction

The uterotubal junction presents anatomical, physiological and/or mucous barriers to sperm passage in most mammals. Anatomically, the lumen in species as distantly related as dairy cattle and mice is particularly tortuous and narrow. The narrowness of the lumen is especially apparent in living tissue and in frozen sections, in which tissue does not shrink as it does during standard preparation of paraffin-embedded sections.

within the lumen of the junction, there are large and small folds in the mucosa. In the cow, mucosal folds form cul-de-sacs with openings that face back towards the uterus. This indicates that normal morphology and motility are not sufficient for enabling sperm to pass through the junction. An additional factor, likely a sperm surface protein or proteins, is required by each sperm for it to pass through the junction.

Rapid sperm transport

Sperm have been recovered in the cranial reaches of the tubal ampulla only minutes after mating or insemination in humans and several other species of mammals. Rapid transport of sperm into the Fallopian tube would seem to counter the proposed model of sperm swimming one-by-one through the uterotubal junction. However, when rabbit sperm recovered from the cranial ampulla shortly after mating were evaluated by Overstreet and Cooper (1978), they found that most were immotile and damaged. They proposed that waves of contractions stimulated by insemination transport some sperm rapidly to the site of fertilization, but these sperm are mortally damaged by the associated sheer stress and do not fertilize. Later, motile sperm gradually pass through the uterotubal junction to establish a tubal population capable of fertilizing. The contractions may serve primarily to draw sperm into the cervix but result in overshooting of some sperm. As described above, motile human sperm have been recovered from Fallopian tubes within an hour of insemination; however, it is not known whether function was normal in these women.ularis to inhibit smooth muscle constriction of the lumen. In each of these cases, the incidence of polyspermy increased.

Sperm binding to endosalpingeal (oviductal) epithelium of non-human eutherian mammals studied to date involves the binding of sperm to carbohydrate moieties on the epithelium. Fetuin and its terminal sugar, sialic acid, were found to competitively inhibit binding of hamster sperm inseminated into oviducts, whereas desialylated fetuin did not. Fetuin binding sites were localized over the acrosomal region of the sperm head, which is the region by which sperm bind to epithelium. Binding of stallion sperm to explants of endosalpinx was inhibited by asialofetuin and its terminal sugar, galactose, while binding of boar sperm was blocked by mannose. Bull sperm binding was blocked by fucoidan and its component fucose and pre-treatment of bovine epithelium with fucosidase reduced binding. In each of the species studied so far, a different carbohydrate inhibited binding in vitro. These species differences may not seem so unusual when one considers that a single amino acid residue can determine the carbohydrate binding specificity of a lectin and that closely related animal lectins have different carbohydrate specificities.

It has not been established whether human sperm attach to the endosalpinx through a carbohydrate, although recent experiments by Reeve et al. (2003) have implicated the amino acid sequence Arg-Gly-Asp (RGD) in sperm binding to isthmic but not ampullary endosalpingeal epithelium. Interestingly, human sperm–endosalpingeal interaction in vitro appears to be disrupted in tissue donated from women who have had a previous diagnosis of endometriosis

Preserving sperm fertility during storage

Sperm–endosalpingeal contact somehow preserves sperm during storage. Human sperm incubated with epithelium in vitro remain viable longer than when they are incubated in medium alone, as do sperm from other mammals. Viability of human sperm and other species can be extended by incubating them with vesicles prepared from the apical membranes of the endosalpinx, indicating that the epithelium can produce the effect by direct contact rather than by secretions. It was reported that equine sperm binding to epithelium or membrane vesicles maintain low levels of cytoplasmic Ca^{2+}, compared to free-swimming sperm or sperm incubated with vesicles made from kidney membranes. Human and equine sperm incubated with endosalpingeal membrane vesicles capacitate more slowly than sperm incubated in capacitating medium alone. Possibly, viability is maintained by preventing capacitation and its concomitant rise in cytoplasmic Ca^{2+}. The mechanism for preventing rises of cytoplasmic Ca^{2+} in sperm are not known, but one suggestion is that catalase, which has been detected in the bovine tube, serves to protect against peroxidative damage to the sperm membranes, perhaps preventing inward leakage of Ca^{2+}.

Taxis of sperm towards oocytes

Although the existence of a guidance system to help mammalian sperm reach the unfertilized oocyte has been debated over the years, stronger evidence for such a system has surfaced recently. There is evidence for the existence of two complementary guidance mechanisms operating within the Fallopian tube. The first (long-range) mechanism is where capacitated sperm—released from intimate contact with the endosalpinx are guided by thermotaxis towards the site of fertilization. A temperature difference of up to 2°C between the cooler tubal isthmus and the warmer tubal ampulla has been detected in rabbits and there are indications that capacitated rabbit sperm tend to swim towards warmer temperatures. Once in the tubal ampulla, and at a closer proximity to the oocyte, a second (short-range) chemotactic mechanism may guide sperm closer to the oocyte.

Sperm are equipped with a mechanism for turning towards the oocyte in response to chemotactic factors; that is, they can switch back and forth between symmetrical flagellar beating and the asymmetrical flagellar beating of hyperactivation. Hyperactivation is reversible, so sperm can alternate between turning and swimming straight ahead. Mammalian sperm have been reported to turn towards, or accumulate in, a gradient of follicular fluid, which could accompany the oocyte into the Fallopian tube. Nevertheless, the chemotactic agent in follicular fluid has not been identified, nor has its presence in the Fallopian tube been detected. Odorant receptors unique to sperm have been localized to a spot on the base of the flagellum of human. Placing human sperm in a gradient of the odorant bourgeonal caused them to orient into the gradient and triggered a calcium and cAMP-mediated signalling cascade. Nevertheless, a chemotactic odorant has yet to be identified in humans or other mammals. If one were found, it could have vast implications for the development of contraceptives, as well as assessment and treatment of infertility.

The fate of non-fertilizing sperm

After fertilization, any sperm remaining in the female reproductive tract may be phagocytosed by isthmic epithelial cells or may be eliminated into the peritoneal cavity where they are phagocytosed. Phagocytosis within the Fallopian tubes may be primarily employed by species, such as mice, which have an extensive ovarian bursa that would limit passage of sperm into the peritoneal cavity. In species where the passage of sperm into the peritoneal cavity is possible, this does not quickly render sperm non-functional as evidenced by the numerous case reports of human tubal pregnancies that arose in spite of lack of access of sperm from the uterus into the oviduct on the side of ovulation.

In summary

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 (oviductal) epithelium. As the time of ovulation approaches, sperm become capacitated and hyperactivated, which enables them to proceed towards the tubal ampulla. Sperm may be guided to the oocyte by a combination of thermotaxis and chemotaxis. Motility hyperactivation 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