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ASSIGNMENT

DISCUSS THE FACTORS FACILITATING THE MOVEMENT OF SPERM IN FEMALE REPRODUCTIVE TRACT

Definition of sperm

Sperm is the male reproductive cell, or gamete, in anisogamous forms of sexual reproduction. Animals produce motile sperm with a tail known as a flagellum, which are known as spermatozoa, while some red algae and fungi produce non-motile sperm cells, known as spermatia.

Sperm cells form during the process known as spermatogenesis, which in amniotes takes place in the seminiferous tubules of the testes. This process involves the production of several successive sperm cell precursors, starting with spermatogonia, which differentiate into spermatocytes. The spermatocytes then undergo meiosis, reducing their chromosome number by half, which produces spermatids. The spermatids then mature and, in animals, construct a tail, or flagellum, which gives rise to the mature, motile sperm cell. This whole process occurs constantly and takes around 3 months from start to finish.

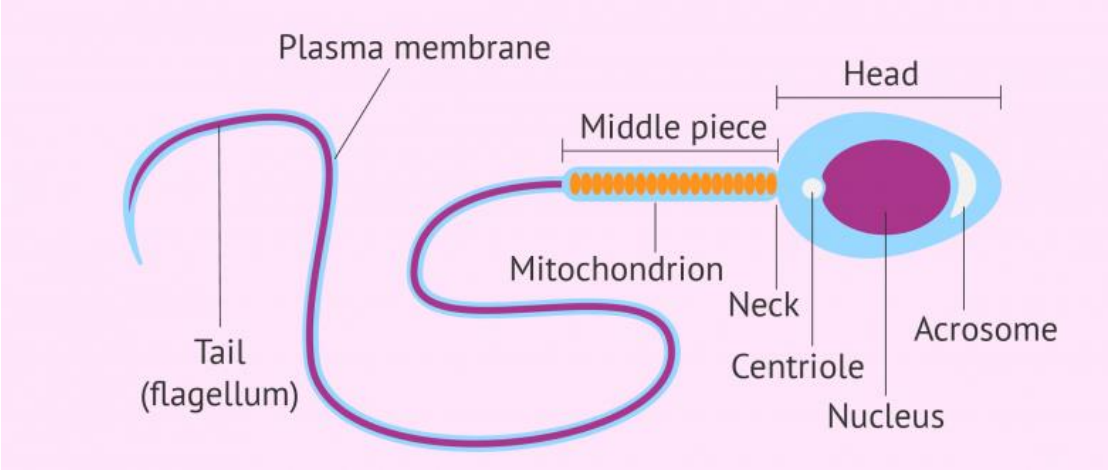

Diagram of a sperm.

Some factors that facilitate the movement of sperm in the female reproductive system includes:

1. Physical interaction

The architecture of cell surfaces can affect the direction of sperm movement. It has long been observed that sperm tend to accumulate at surfaces, particularly the surfaces of slides and coverslips. When sperm that are swimming along a flat horizontal surface reach a side wall, they tend to continue swimming along the corner where the two walls meet . The surfaces of the walls of the female reproductive tract are, of course, far more complex in design than the surfaces of microscope slides. Recently, Denissenko and colleagues took advantage of advances in microtechnology to construct micro channels of various configurations to test how angles and curved surface would affect movement of sperm. These micro channels were constructed of polymethylsiloxane (PDMS), which is a somewhat soft and elastic silicon based polymer that more closely resembles the properties of epithelial surfaces than do glass slides, but is also optically clear. They observed that when human sperm that were swimming along a surface encountered a sharp outward turn, the sperm would leave the surface until they encountered another surface. Using this information, they constructed a “one-way running track” for sperm. When human sperm were loaded into this circular channel with scalloped walls, they tended to swim in a counterclockwise direction around the circle . It is very interesting that a scanning electron micrograph of the inner surface of the bovine uterotubal junction reveals shapes that resemble the architecture of the running track. This resemblance indicates that the micro architectural of the junctional walls could guide sperm to swim toward the oviduct.

Site of semen deposition

The site of semen deposition is not easy to establish in many species because it must be determined by examining the female immediately after coitus and by considering the anatomy of the penis, vagina and cervix during coitus. However, it has been accomplished for humans, in which semen has been observed pooled in the anterior vagina near the cervical os shortly after coitus. Within minutes of vaginal deposition, human sperm begin to leave the seminal pool and swim into the cervical canal. In contrast, rodent sperm deposited in the vagina are swept completely through the cervix into the uterus along with seminal plasma within a few minutes. Some species, such as pigs, bypass the vagina altogether and deposit semen directly into the uterine cavity, where sperm may quickly gain access to the oviduct.

Whereas most of the semen of murine rodents is rapidly transported into the uterine cavity, some remains in the vagina where it coagulates to form a copulatory plug. The plug forms a cervical cap that promotes sperm transport into the uterus. Ligation of the vesicular and coagulating glands of rats prevented the formation of plugs and the transport of sperm into the uterus. The plugs formed by semen of guinea pigs and mice extend into the cervical canals and thus could form a seal against retrograde sperm loss.

Male mice deficient for the gene encoding the protease inhibitor known as protease nexin-1 (PN-1) show a marked impairment in fertility. Vaginal plugs formed in females after mating with PN-1 null males were small, soft and fibrous and did not lodge tightly in the dual cervical canals. No sperm could be found in the uterus 15 min after mating with PN-1 null males, demonstrating the importance of the plug for promoting transport of mouse sperm into the uterus.

Human semen coagulates, but it forms a loose gel rather than the compact fibrous plug seen in rodents. The coagulate forms within about a minute of coitus and then is enzymatically degraded in to 1 h. The predominant structural proteins of the gel are the 50 kDa semenogelin I and the 63 kDa semenogelin II, as well as a glycosylated form of semenogelin II, all of which are secreted primarily by the seminal vesicles. The gel is degraded by prostate-specific antigen (PSA), a serine protease secreted by the prostate gland (Watt et al., 1986). It has been proposed that this coagulum serves to hold the sperm at the cervical os and that it protects sperm against the harsh environment of the vagina.

Seminal gels are not fully successful at holding sperm at the cervical os. In cattle, several studies have demonstrated loss of sperm from the vagina after mating or insemination. The fate of spermatozoa that are ejaculated or inseminated into the vagina, but that do not enter the cervix, has not been studied extensively in humans. However, in a 5 year study of 11 female volunteers Baker and Bellis examined

the characteristics of sperm loss from the vagina following coitus. They found that flow back occurred in 94% of copulations with the median time to the emergence of ‘flow back’ of 30 min (range 5–120 min). Furthermore they estimated that a median of 35% of spermatozoa were lost through flow back but that in 12% of copulations almost 100% of the sperm inseminated were eliminated. This suggests that less than 1% of sperm might be retained in the female reproductive tract and this supports the notion that only a minority of sperm actually enter cervical mucus and ascend higher into the female reproductive tract.

Like humans, some primates produce semen that forms a soft gel. However, in chimpanzees, a species in which females mate with more than one male in a brief time, the semen coagulates into a compact plug resembling that of rodents. The plug may serve to prevent other males from mating with the female. Some carnivores (e.g. domestic dogs, Canis familiaris) and some rat and mouse species of the family Cricetidae use the penis as a copulatory plug; i.e. the mating pair remains joined together for a period after coitus.

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. Radio opaque 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 cervices 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 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.

Immunoglobulins, IgG and IgA, have been detected in human cervical mucus. Secretory IgA is produced locally by plasma cells in subepithelial connective tissue. The amount secreted increases in the follicular phase but then decreases at about the time of ovulation. The immunoglobulin's 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 also present in cervical mucus, along with regulators of complement activity. Thus, there is a potential for antibody-mediated destruction of sperm in the cervical mucus as well as leukocytic capture of sperm. Some anti-sperm antibodies are not complement-activating; however, they can still interfere with movement of sperm through cervical mucus by physical obstruction.

An elegant three-dimensional reconstruction of serial sections of the bovine cervix produced by Mullins and Saacke led them to conclude that mucosal folds in the cervical canal form channels leading to the uterine cavity. Furthermore, based on histochemical staining characteristics of the mucus, they concluded that, during the follicular phase, mucus deep in the channels is different in composition and less dense than that in the central portion of the cervical canal. They proposed that bull sperm enter deep channels at the external os and travel in them all the way to the uterine cavity, thereby avoiding the more viscous mucus in the center of the cervical canal that serves to discharge uterine contents. This model is supported by results of earlier studies on farm animals. Mattner found that when he flushed the cervices of goats and cows 19–24 h after mating he recovered approximately 90% of the mucus and more

than 90% of the luminal leukocytes, but only about half of the sperm. The remaining half of the sperm were found deep in the mucosal grooves. These observations also indicate that the cervix supports the passage of normal motile sperm while discouraging passage of microbes and sperm with abnormal form or motility. Normal, fresh, motile sperm can avoid the area most populated by neutrophils and they appear to be resistant to leukocytic phagocytosis anyway, as discussed above. In descriptions of human cervical anatomy, mention is made of cervical crypts that are thought to entrap and store sperm. On the other hand, scanning electron microscopy of the human cervix indicates that mucosal grooves forming a preferential pathway for sperm could be present as in the bovine. A comprehensive study of the human cervix is needed to determine whether sperm follow mucosal grooves to traverse the cervical canal.

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 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.

Sperm transport through the uterus

At only a few centimeters 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 fimbria 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 per ovulatory 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.

In humans, contractile activity of uterine muscle may draw sperm and watery midcycle mucus from the cervix into the uterus. Fukuda and Fukuda interpreted ultrasound images of the uteri of women in the late follicular phase to indicate that the uterine cavity is filled with mucus. They proposed that the cervical mucus assists sperm movement through the human uterine cavity. This is possible because the volume of uterine fluid in midcycle women is only about 100 µl and cervical mucus is plentiful enough to fill the lumen. A scanning electron micrograph of the human cervix, illustrating potential passageways for sperm (×67). A portion of the wall has been removed to reveal the architecture of the cervical canal (CC). Large, primary mucosal grooves (PG) can be seen at the external os that extend deep into the cervical canal. Smaller secondary mucosal grooves (SG) branch from the primary grooves. Although the primary grooves appear to form a preferential path for sperm, it is not known whether secondary or even tertiary grooves could end blindly and entrap sperm. Cervical crypts could also trap sperm. Reproduced, with permission, from Kessel and Kardon.

Kunz and collaborators deposited 5–40 µm albumen microspheres radioactively tagged with technetium into the cranial vaginae of women to determine how such contractions might transport sperm. They found that spheres were rapidly and maximally transported into the uterine cavity and even into the tubal isthmus during the late follicular phase. Interestingly, transport of the spheres was greater to the isthmus ipsilateral to the dominant follicle than to the contralateral isthmus. This preferential transport may result from signals passed through a vascular communication from the pre-ovulatory follicle to the uterus and Fallopian tube. An arterial anastomosis lies between the ovarian and uterine arteries (which also supply the Fallopian tube) in the corneal region of the human uterus. Doppler flow sonography

revealed increased perfusion of these anastomosing vessels on the side of the pre-ovulatory follicle. It is thought that these vessels carry hormones from the dominant follicle directly to the uterus and oviduct without first passing through the systemic circulation, because the ovarian artery associates closely with the ovarian vein. This could enable a countercurrent transfer of ovarian hormones from the venous drainage

of the ovary to the ovarian artery and then to the arterial supply of the uterus and oviduct. In addition, lymphatic drainage of the ovary might transfer hormones to the ovarian artery and then the oviduct vessels.

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.

Myometrium 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 myometrium 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 of PGF-2α.

Rapid transport of sperm through the uterus by myometrial contractions can enhance sperm survival by propelling them past the immunological defenses of the female. As is the case in the vagina and cervix, coitus induces a leukocytic infiltration of the uterine cavity, which reaches a peak several hours after mating in mice. The leukocytes are primarily neutrophils and have been observed phagocytizing uterine sperm in mice, rats and rabbits. This phagocytosis was observed several hours after insemination and therefore might be directed primarily against damaged sperm. However, normal sperm may also be attacked, particularly in vaginal inseminators like humans, because their sperm have lost much of the immune protection afforded by seminal plasma constituents. 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 paraffinembedded sections.

The entrance to the junction is fairly simple in humans; whereas, it is complicated by mucosal folds in cows, pigs, rabbits and many other species. In mice and rats, the entrance forms a conical projection into the uterus called a colliculus tubarius. 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 arrangement of folds seems designed to entrap sperm and prevent further ascent.

A physiological valve may be created by a vascular plexus in the lamina propria/sub mucosal layer of the wall. When engorged, the plexus can compress the lumen. This plexus has been well described in cattle. The walls of the bovine junction and adjacent tubal isthmus also contain a thick muscular layer that could further constrict the lumen. The bovine uterotubal junction is sigmoidal in shape and supported by muscular ligaments that appear capable of increasing the flexure of the curve and thus compressing the lumen. In the mouse, the junction is reported to be patent shortly after coitus, but to be tightly closed about an hour later. The human junction traverses a thick muscular layer of uterine wall; however, it is unknown whether the muscle regulates the patency of the junction.

The narrow lumen of the uterotubal junction may be filled with viscous mucus that can impede the progress of sperm. Mucus has been found in the uterotubal junction in humans, as well as in rabbits, pigs and dairy cattle. In rodents, it has been demonstrated that sperm with linear, progressive motility are more successful at passing through the uterotubal junction.

Male mice that are null mutants for the genes encoding fertilin β, calmegin or testis-specific angiotensin converting enzyme (ACE) are infertile because their sperm cannot pass through the uterotubal junction nor bind to the zona pellucida. In these null mutants, both the motility and morphology of the sperm are normal. Fertilin β is localized on the plasma membrane overlying the acrosome on mature sperm from wild-type males, while it is lacking in the null mutants. As for calmegin, sequence homology indicates that it is a chaperone protein, which would place it in the endoplasmic reticulum of spermatids, assisting in the proper folding of proteins destined for membranes. Both wild-type and null mutants lack calmegin in mature sperm; therefore, its effect on fertility is presumed to be due to the lack of proteins that rely on calmegin for proper placement in the sperm plasma membrane. In the case of ACE null mutants, there is strong evidence that the missing ACE normally acts to release GPI-anchored proteins from the sperm plasma membrane. Thus, the

lack of ACE means that some proteins that would normally be shed from sperm are retained. These various strains of null mutant mice indicate that certain epitopes must be available and exposed on the surface of sperm to interact with the uterotubal junction and somehow promote sperm passage.

The role of calmegin in enabling sperm to pass through the uterotubal junction was examined more closely using chimeric males that produced a mixture of germ cells with wild-type and disrupted calmegin genes. The question addressed was whether calmegin-chaperoned proteins are required by individual sperm to pass through the junction, or would the presence of wild-type sperm enable them to do so. Such would be the case, for example, if the proteins on the sperm surface assist passage by signaling the junction to open. Chimeric males were created by fusing embryos from 'wild-type' mice that had normal calmegin genes with those from a double transgenic line of mice that were homozygous null for calmegin and expressed enhanced green fluorescent protein (GFP) in their acrosomes. The resulting chimeric XY/XY males produced a mixture of sperm, about half of which were mutant, as identified by the presence of the fluorescent acrosomes. When these males were mated with wild-type females, only wild-type sperm could be found above the junction. 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, 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.

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 Ca2+, compared to freeswimming 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 Ca2+. The mechanism for preventing rises of cytoplasmic Ca2+ 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 Ca2+.

The endosalpingeal binding protein on bull sperm, PDC-109, probably acts to stabilize sperm membranes. PDC-109 reduces membrane fluidity and immobilizes cholesterol in phospholipid membranes, including those of epididymal sperm. PDC-109 can also contribute to membrane stability by inhibiting the activity of phospholipase A2. Thus, PDC-109 may play a role in preserving bull sperm fertility while they are stored in the reservoir. Homologues to PDC-109 have been identified in many species; however, a functional equivalent has yet to be identified in humans.

Hyper activation of sperm and the final stages of transport

At some point in the female tract, most likely in the Fallopian tubes, sperm become hyper activated. In aqueous media in vitro, hyper activated sperm swim vigorously but in circular or erratic patterns. In vivo, the physical environment encountered by sperm is quite different and evidence indicates that hyper

activation is required by sperm to progress towards the oocyte and penetrate its vestments. As discussed above, hyper activation may assist sperm in detaching from the endosalpingeal epithelium. In addition, hyper activation enhances the ability of sperm to swim through viscoelastic substances such as mucus in the tubal lumen and the extracellular matrix of the cumulus oophorus. Mucus fills the uterotubal junction and extends into the isthmus in humans, rabbits, pigs and dairy cattle. Hyper activated sperm penetrate artificial mucus, such as viscoelastic solutions of long-chain polyacrylamide or methylcellulose, far more effectively than non-hyper activated sperm.

Hyper activation also endows sperm with greater flexibility for turning around in pockets of mucosa. In the human Fallopian tube, as discussed above, mucosal folding

increases in height and branching from the isthmus to the ampulla and thus hyper activation may assist sperm in navigating the increasingly complex maze .The most convincing evidence of the importance of hyper activation in these final stages of a sperm's journey comes from experiments with mice in which the gene for CatSper1 or CatSper2 has been disrupted. Sperm from these animals do not reach the oocytes in the oviductal ampulla. Although they show normal vigorous progressive motility, they cannot hyper activate and do not penetrate artificial mucus as well as wild-type sperm.

In addition to assisting sperm in reaching the oocyte, hyper activation also aids sperm in penetrating the zona pellucida. When hyper activation was blocked in capacitated, acrosome-reacted hamster sperm bound to the zona, they were unable to penetrate it. Also, sperm from male mice that are null mutants for CatSper1 or CatSper2 genes and cannot hyper activate also cannot penetrate the zona.

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 hyper activation. Hyper activation is reversible, so sperm can alternate between turnings 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, canine and rat sperm. Placing human sperm in a gradient of the odorant bourgeonal caused them to orient into the gradient and triggered a calcium and cAMP-mediated signaling 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 phagocytized by isthmic epithelial cells or may be eliminated into the peritoneal cavity where they are phagocytized. 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 these cases, the only route available to the sperm was through the peritoneal cavity