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QUESTION

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

Transport of sperm from site of deposition in the female to site of fertilization represents a critical phase of the reproductive process of mammals. Sperm transport failures, which result in fertilization failure, account for a significant proportion of the loss of potential offspring in each major class of animal. The term "sperm transport" properly means the movement of sperm by the female reproductive tract from the site of deposition of semen to the ampulla of the oviducts. However, the term often is used in a broader sense to define movement of sperm in the female regardless of whether the movement resulted from action of the female tract or from action of sperm.

The mammalian female reproductive tract interacts with sperm in various ways in order to facilitate sperm migration to the egg while impeding migrations of pathogens into the tract, to keep sperm alive during the time between mating and ovulation, and to select the fittest sperm for fertilization. The two main types of interactions are physical and molecular. Physical interactions include the swimming responses of sperm to the microarchitecture of walls, to fluid flows, and to fluid viscoelasticity. When sperm encounter walls, they have a strong tendency to remain swimming along them. Sperm will also orient their swimming into gentle fluid flows. The female tract seems to use these tendencies of sperm to guide them to the site of fertilization. When sperm hyperactivate, they are better able to penetrate highly viscoelastic media, such as the cumulus matrix surrounding eggs. Molecular interactions include communications of sperm surface molecules with receptors on the epithelial lining of the tract. There is evidence that specific sperm surface molecules are required to enable sperm to pass through the uterotubal junction into the oviduct. When sperm reach the oviduct, most bind to the oviductal epithelium. This interaction holds sperm in a storage reservoir until ovulation and serves to maintain fertilization competence of stored sperm. When sperm are released from the reservoir, they detach from and re-attach to the epithelium repeatedly while ascending to the site of fertilization. We are only beginning to understand the communications that may pass between sperm and epithelium during these interactions.

That is, the male transfers sperm into the female reproductive tract and then the sperm must migrate through a portion of the tract in order to reach eggs and fertilize them.

Evolution of the female reproductive tract seems to be driven by a number of factors. One is the need to facilitate sperm migration to the egg while impeding migration of pathogens into the tract. Another is that the female tract must be able to keep sperm alive for hours, days, or even months, depending on the period between the optimal time to mate and the optimal time to initiate development of an embryo. In addition, it is believed that the female employs a strategy to attempt to select the fittest sperm for

fertilization. Given all of these factors that operate on the process of reproduction, it should not be surprising that the female reproductive tract interacts in various ways with sperm in order to facilitate migration to the egg, store sperm until needed, and select sperm of the best quality to fertilize.

There are two main categories of interactions of sperm with the female reproductive tract, namely, physical and molecular. The physical category includes the swimming responses of sperm to the microarchitecture of the walls of the tract, to fluid flows, and to fluid viscoelasticity. Molecular interactions include communications of sperm surface molecules with receptors in the epithelial linings of the tract. Indirect molecular interactions, such as effects of tract secretions on sperm, effects of seminal plasma on the tract, or interactions of sperm with immune cells that enter the lumen of the tract will not be discussed in this review.

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 scientists took advantage of advances in microtechnology to construct microchannels of various configurations to test how angles and curved surface would affect movement of sperm. These microchannels were constructed of polymethyl siloxane (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 microarchitectural of the junctional walls could guide sperm to swim toward the oviduct.

The fertilizing capacity of sperm may be maintained by their interaction with oviductal epithelium. For example, bull sperm fertility and motility are maintained longer *in vitro* by incubation with oviductal epithelium. Holding sperm in the lower oviduct may also serve to prevent polyspermic fertilization by allowing only a few sperm at a time to reach oocytes in the ampulla. Sperm numbers were experimentally increased at the site of fertilization in the pig by surgically inseminating sperm directly into the oviduct, by surgically removing the region of the reservoir and reconnecting the remaining tube, or by injecting

progesterone into the oviduct wall to inhibit smooth muscle constriction of the tube. Each of these treatments raised the incidence of polyspermic fertilization.

Hyperactivation of Motility

This is described as one of the hallmark characteristic changes seen as a result of capacitation. Sperm motility becomes more vigorous with a decreased rate of forward progression. Specifically, the sperm develops:

- Wider amplitude of lateral head displacement
- Marked increase in flagellar beating
- A curved and tortuous trajectory⁷⁹

Although the functional significance of these changes remains unclear, they may facilitate sperm transit through the oviduct and provide the necessary force needed to penetrate the granulosa cell layer and zona pellucida surrounding the ovum.^{69A,70A} Some studies have shown hyperactivation in about 20% of spermatozoa after a sufficient incubation period with in vitro media, and sperm that display hyperactivated patterns tended to be those with normal morphology.⁸⁰ Factors determining which sperm incubated in capacitating solutions will ultimately demonstrate hyperactive motility are not well understood.

Sperm Membrane Changes

The sperm plasma membrane is composed of a lipid bilayer interspersed with a number of proteins. Lipid types present include cholesterol, glycolipids, and phospholipids. The proteins found here can traverse the entire membrane from cytosolic compartment to extracellular space. These proteins have important functions, including activation of receptors and transport of ions.

Fertilization is a numbers game. During ejaculation, hundreds of millions of sperm (spermatozoa) are released into the vagina. Almost immediately, millions of these sperm are overcome by the acidity of the vagina (approximately pH 3.8), and millions more may be blocked from entering the uterus by thick cervical mucus. Of those that do enter, thousands are destroyed by phagocytic uterine leukocytes. Thus, the race into the uterine tubes, which is the most typical site for sperm to encounter the oocyte, is reduced to a few thousand contenders. Their journey—thought to be facilitated by uterine contractions—usually takes from 30 minutes to 2 hours. If the sperm do not encounter an oocyte immediately, they can survive in the uterine tubes for another 3–5 days. Thus, fertilization can still occur if intercourse takes place a few days before ovulation. In comparison, an oocyte can survive independently for only approximately 24

hours following ovulation. Intercourse more than a day after ovulation will therefore usually not result in fertilization.

During the journey, fluids in the female reproductive tract prepare the sperm for fertilization through a process called capacitation, or priming. The fluids improve the motility of the spermatozoa. They also deplete cholesterol molecules embedded in the membrane of the head of the sperm, thinning the membrane in such a way that will help facilitate the release of the lysosomal (digestive) enzymes needed for the sperm to penetrate the oocyte's exterior once contact is made. Sperm must undergo the process of capacitation in order to have the "capacity" to fertilize an oocyte. If they reach the oocyte before capacitation is complete, they will be unable to penetrate the oocyte's thick outer layer of cells.