

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. Knowledge of the biology of sperm transport can inspire improvements in artificial insemination, IVF, the diagnosis of infertility and the development of contraceptives.

Sperm transport within the female reproductive tract is a cooperative effort between the functional properties of the sperm and seminal fluid on the one hand and cyclic adaptations of the female reproductive tract that facilitate the transport of sperm toward the ovulated egg. Much of the story of sperm transport in the female reproductive system involves the penetration by the sperm of various barriers along their way toward the egg (see Fig. 14.7B).

During coitus in the human, semen is deposited in the upper vagina close to the cervix. The normal environment of the vagina is inhospitable to the survival of sperm, principally because of its low pH (<5.0). The low pH of the vagina is a protective mechanism for the woman against many sexually transmitted pathogens, because no tissue barrier exists between the vagina (outside) and the peritoneal cavity (inside). The acidic pH of the vagina is bacteriocidal and is the reflection of an unusual functional adaptation of the vaginal epithelium. Alone among the stratified squamous epithelia in the body, the cells of the vaginal lining contain large amounts of glycogen. Anaerobic lactobacilli within the vagina break down the glycogen from shed vaginal epithelial cells, with the production of lactic acid as a byproduct. The lactic acid is responsible for the lowered vaginal pH. Direct measurements have shown that within 8 seconds from the introduction of semen the pH of the upper vagina is raised from 4.3 to 7.2, creating an environment favorable for sperm motility. Another rapid event is the coagulation of human semen through the actions of semogelin by a minute after coitus. The coagulative function is incompletely understood, but it may play a role in keeping sperm near the cervical os. Thirty to 60 minutes after it coagulates, prostate-specific antigen (PSA), a proteolytic enzyme, degrades the coagulated semen. Within the semen and altered vaginal fluids, the sperm have begun to swim actively. A critical element in sperm motility is the availability of fructose, a nutrient provided by the seminal vesicles, within the semen. Because of their paucity of cytoplasm, spermatozoa require an external energy source. Unusually for most cells, spermatozoa have a specific requirement for fructose rather than glucose, the more commonly utilized carbohydrate energy source.

The next barrier facing sperm is the cervix. The cervical entrance (os) is not only very small, but it is blocked by cervical mucus. During most times in the menstrual cycle, cervical mucus is highly sticky (G mucus) and represents an almost impenetrable barrier to sperm penetration. Around the time of ovulation, however, the estrogenic environment of the female reproductive system brings about a change in cervical mucus, rendering it more watery and more amenable to penetration by sperm (E mucus).

Considerable uncertainty surrounds the question of passage of sperm through the cervix. The swimming speed of human sperm in fluid is approximately 5 mm/min, so in theory, sperm could swim through the cervical canal in a matter of minutes or hours. In reality, some sperm have been found in the upper reaches of the uterine tubes within minutes of coitus. These pioneers are likely to have been swept up the female reproductive tract during muscular contractions occurring at the

time of or shortly after coitus. Research on rabbits has indicated that most of these sperm have been damaged and would not be able to fertilize an egg. The functional status of early-arriving human sperm is not known. On the other end of the spectrum, viable sperm have been taken from the cervix as long as 5 days after coitus. Between these two extremes, over the course of hours or even days, most of the spermatozoa make their way through the cervical mucus and up the cervical canal and into the uterus, where even less is known about the course of sperm transport in the human. Whether or not sperm are stored in the cervix is still not entirely certain. Sperm transport into and through the uterus is assumed to be assisted by contractions of its thick smooth muscle walls. There may or may not be subtle influences that favor the transport of sperm toward the opening of the uterine tube that contains the ovulated egg.

Of the huge numbers of sperm that enter the female reproductive tract, almost all fail to reach the uterine tubes. The unsuccessful sperm are removed by the infiltration of white blood cells into the cavities of the vagina, cervix, and uterus. These cells, along with certain immunoglobulins, inactivate and degrade foreign invaders, in this case, the excess sperm. Fortunately, the uterine tubes are not subject to this sort of cellular infiltration.

The openings of the uterine tubes into the uterus (uterotubal junction) represent another barrier to sperm transport. With two uterine tubes and usually only one ovulated egg, any spermatozoon that enters the empty uterine tube is automatically doomed to reproductive failure. Roughly 10,000 or fewer sperm cells of the millions in the ejaculate enter the correct tube. These sperm cells collect in the lower part of the uterine tube and attach to the epithelium of the tube for about 24 hours. Two critical events occur during this period of attachment. The first is called capacitation, a reaction necessary for a spermatozoon to be able to fertilize an egg. The first phase of the capacitation reaction is the removal of cholesterol from the surface of the sperm. Cholesterol was introduced onto the sperm head to prevent premature capacitation. The next phase of capacitation is the removal of many of the glycoproteins that were deposited on the sperm head within the epididymis. After their removal, the spermatozoon is now capable of fertilizing an egg. It is likely that covering the sperm cells with glycoproteins and then cholesterol is done to prevent the sperm from prematurely attempting to fertilize other somatic cells that they encounter on their way to meeting the egg. Capacitation removes the molecular shield.

A second phenomenon occurring while the sperm are attached to the distal tubal lining is hyperactivation of the sperm. Hyperactivation is manifest by the increased vigor in their swimming movements and allows the sperm to break free from their binding with the tubal epithelial cells. Hyperactivated sperm are more efficient in making their way up the uterine tube and penetrating the coverings of the egg.

Once capacitated sperm break away from the tubal epithelium, they make their way up the uterine tube through a combination of their own swimming movements, peristaltic contractions of the smooth musculature of the tubal wall and the movement of tubal fluids directed by ciliary activity. In the upper third of the uterine tube, a few hundred sperm approach the ovulated egg. Only one of them out of the millions that left the male reproductive tract will attain its ultimate goal of fertilizing that egg.