THE EGG DECIDES WHICH SPERM FERTILIZES IT



By <u>Dr. Ananya Mandal, MD</u>Jun 11 2020

There is ample evidence to show that as millions of human sperm cells swim towards a waiting ovum or egg, only one gets to fertilize it. Now, a new study shows that even though the fastest and most capable sperms reach the ovum first, it is the egg that has the final say on which sperm fertilizes it. The study titled, "Chemical signals from eggs facilitate cryptic female choice in humans," is published in the latest issue of the journal *Proceedings of the Royal Society B*.

What is the study about?

This new study by researchers from the U.K. and Sweden looked at the dynamics between the waiting ovum and the sperms that swim towards it. The team says that there is a chemical communication that occurs between the female reproductive system that receives the sperm and the incoming sperm cells from the male partner. They explained that the primary mechanism might be known, but the molecular mechanism that forms the basis of choice of sperm cell by the egg is not clear. They write, "there is a growing appreciation that females can bias sperm use and paternity by exerting cryptic female choice for preferred males."

The team from Stockholm University and Manchester University NHS Foundation Trust speculates that there may be chemicals that attract the sperm. These chemo-attractants are released from the eggs, they wrote. These allow the egg to choose between the sperms swimming towards them. This post-mating choice of sperms has been seen in some species. This study looked at similar findings among humans.

What was done?

For this study, the team assayed the mate choice microscopically. They assessed the "gamete mediate mate choice." This essentially means the egg chooses the sperm cell. They explained that once the sperm is released in the female reproductive tract, they start to swim towards the ovum. Only around a few hundred sperms reach the follicles or tubes. There it meets the follicular fluid, which has these chemo-attractants.

They looked at the effects of follicular fluid present in the female reproductive system on the incoming sperms. The team wrote that this fluid in the follicles or tubes is known to have certain chemo-attractants which attract the sperms. They used follicular fluids from the female partner and exposed the sperms to these fluids. Both partners (the male partner of the female whose follicular fluid was tested) and non-partner (another male) sperms were exposed to the follicular fluid of a female. For this study, the researchers used the follicular fluids and sperms from six couples who were undergoing treatment for infertility.

What was found?

This study found that there is a marked differentiation between the attractions from the follicular fluid of a female partner compared to the follicular fluid of a non-partner for the sperm cells. This indicated that there is a distinct mate choice when it comes to eggs and sperms. This, however, did not influence "pre-mating mate choice" in humans, they wrote.

Study author John Fitzpatrick, Associate Professor at Stockholm University, explained, "Human eggs release chemicals called chemo-attractants that attract sperm to unfertilized eggs. We wanted to know if eggs use these chemical signals to pick which sperm they attract."

Fitzpatrick explained that when the sperms they experimented with travel into the follicular fluids of their partner females, "they start to go straighter, and they start to change the way they swim." He added, "So depending on the strength of that signal, you can get different responses in how the sperm are responding to these female chemical signals within their follicular field." The sperm slows down if the follicular fluid is not conducive to it.

Conclusions and implications

The researchers wrote, "Our results demonstrate that chemo-attractants facilitate gametemediated mate choice in humans, which offers females the opportunity to exert cryptic female choice for sperm from specific males."

Fitzpatrick added, "Follicular fluid from one female was better at attracting sperm from one male, while follicular fluid from another female was better at attracting sperm from a different male.... This shows that interactions between human eggs and sperm depend on the specific identity of the women and men involved."

The researchers believe that this study and the understanding of how the sperms fertilize eggs could help couples with infertility. Choosing sperms that are compatible with the follicular fluid could help. "Eggs attracting around 18 percent more sperm from specific males would likely be pretty important during fertilisations inside the female reproductive tract", since only a small fraction of sperm reach the egg after sex, said Fitzpatrick. He said that there may be a chemical incompatibility between the sperms and the follicular fluid that made it difficult for couples to conceive. Fitzpatrick said, "We weren't considering how chemical signals might influence egg-sperm interactions before. Our work helps open the door to consider this in the future."

Professor Daniel Brison, the scientific director of the Department of Reproductive Medicine at Saint Marys Hospital, senior author of the study, said, "The idea that eggs are choosing sperm is really novel in human fertility." He added, "Research on the way eggs and sperm interact will advance fertility treatments and may eventually help us understand some of the currently 'unexplained' causes of infertility in couples." He said, "I'd like to thank every person who took part in this study and contributed to these findings, which may benefit couples struggling with infertility in future." One in ten couples suffer from fertility issues, say researchers.

A WOMAN'S EGGS CHOOSE LUCKY SPERM DURING LAST MOMENTS OF CONCEPTION, STUDY FINDS

In females, for example, hormones present at ovulation can drive a woman to choose a <u>cocky</u>, <u>confident man</u> with a <u>slight stubble and more masculine features</u>. Men can sniff out an ovulating woman just by <u>smelling her T-shirt</u>, while <u>women appear to prefer the smell of a man with</u> <u>dissimilar genes</u>, which could give her offspring a boost up the evolutionary ladder.



Boosting male fertility with diet and weight loss

A fascinating new study finds those chemical-based preferences continue even after sex. Human eggs appear to "choose" which sperm will become the lucky winner in conceiving a baby.

"Human eggs release chemicals called chemoattractants, which leave a sort of chemical breadcrumb trail that sperm use to find unfertilized eggs," said study author John Fitzpatrick, an assistant professor in the department of zoology at Stockholm University in Sweden.

"What we didn't know until this study is those chemical breadcrumbs act differently on sperm from different males, in effect choosing which sperm is successful," Fitzpatrick added.

"What this is suggesting is that these fluids are giving females one extra chance — long after she's picked her partner — to bias the number of sperm that are going to be coming towards the eggs."

And here's the extraordinary finding: A woman's egg doesn't always agree with her choice of partner.

"We expected to see some sort of partner effect, but in half of the cases the eggs were attracting more sperm from a random male," Fitzpatrick said. "The most likely explanation for this is that these chemical signals allow females to choose males who are more genetically compatible."

The hunt for diverse genes

What makes a partner genetically compatible? One of the driving factors for that, Fitzpatrick said, are a complex set of genes called the "major histocompatibility complex," or MHC for short.

"Basically what these genes are about is fighting infection, fighting diseases and helping our immune system do really well," he said. "The more diverse those genes are, the more diverse are the kinds of infections you can fight. And if your partner has a slightly different combination of these genes than you do, then you're going to produce offspring that can fight an even broader array of pathogens and diseases."

And because mammals, including humans, are programmed to give our offspring the best chance for survival, our bodies have developed all sorts of methods to reward the strongest, most diverse and compatible mate possible. Even the female reproductive tract is an obstacle course designed to weed out weaker, less acceptable suitors.

Reproductive tract fluids, for example, flow downwards, thus forcing sperm to swim upstream, much like salmon must do when they spawn. At the same time, Fitzgerald said, the female's immune system views sperm as a foreign invader, attacking those swimmers as if they were germs. Once past the obstacle of the cervix's muscular contractions, sperm must then choose and swim up one of two fallopian tubes — yet the egg only travels down one, leaving a "blind alley that they can go down where there's no payoff."

The journey is so arduous that of the tens of millions of sperm a male might deposit, "our best estimate is that only about 250 total sperm get to the site of fertilization where the egg is," Fitzgerald said.

"On top of all of that, only about 10% of the 250 sperm are able to fertilize at any given time — they sort of blink on and off in their capacity to fertilize eggs," he added."So of that 250, it's more like 20 or 30 cells that can actually fertilize an egg at any different time."

Finally, the egg can affect which sperm wins the race with the chemicals it releases in the follicular fluid that surrounds the egg. That's the part which contains the chemical breadcrumbs eggs use to attract and guide sperm to their goal.

"And it's only in the last two centimeters betwen a sperm and the egg that these chemical signals matter since it's the final phase of this long journey where females continue weeding out less acceptable sperm," Fitzgerald said.

At this point, he added, "we're talking some real numbers that could have an important impact on fertility."

A test tube study

The study, published Tuesday in the journal Proceedings of the Royal Society, used left over follicular fluid and sperm samples from 16 couples undergoing assisted reproductive treatment at St. Mary's Hospital in Manchester, England.

Experiments were carried out on fluids and sperm of two couples at a time, exposing sperm from each male to follicular fluid from their partner and a non-partner on several occasions. Sperm had to swim the length of a microcapillary tube across the petri dish; the number of those that made the journey successfully were then counted.

The study discovered that that eggs attract between 18% and 40% more sperm from the preferred male. How?

Sperm, as it turns out, have odor receptors in their heads that respond to the chemoattractants in the egg's follicular fluid, thus influencing how vigorously the sperm swims.

"So when sperm go into the follicular fluid, they start to go straighter and they start to change the way they swim," Fitzgerald said. "So depending on the strength of that signal, you can get different responses in how the sperm are responding to these female chemical signals within their follicular field."

If the egg wants the sperm to swim in the "fast lane," so to speak, it will send chemicals to encourage that. If it doesn't, it may send chemicals to slow the sperm's pace.

"That's a really good analogy because in some cases the female's follicular fluid is going to make one male sperm do the speedy front crawl and then another male sperm do the backstroke," Fitzgerald said. "The idea that eggs are choosing sperm is really novel in human fertility," said senior author Daniel Brison, the scientific director of the department of reproductive medicine at Saint Mary's Hospital in the UK, which is part of the Manchester University NHS Foundation Trust. "Research on the way eggs and sperm interact will advance fertility treatments and may eventually help us understand some of the currently 'unexplained' causes of infertility in couples," Brison said in a statement.

About a third of all cases of clinical infertility have unexplained causes, Fitzgerald said, adding that now that "we know that eggs are exerting some sort of control on sperm, we can start looking at that and start to narrow down that 30% of unexplained cases."

"We've known for a long time that one or more components of follicular fluid may be important in helping the sperm find the egg, but to my knowledge it's the first time that anyone has suggested that there might be some sperm-follicular fluid combinations that are better than others. That's intriguing," said Allan Pacey, a professor of andrology at the University of Sheffield in the UK, who was not involved in the study.

Couples who are currently experiencing infertility, however, shouldn't worry about whether or not they have sperm and follicular fluid compatibility problems, he added.

"Whilst the results of this study are very interesting and the experiments elegantly performed, I am not sure whether they currently have any clinical relevance for anyone concerned about their fertility or undergoing IVF [in vitro fertilization]," Pacey said. "But they may well give researchers a better handle on how human sperm and eggs meet, and why that sometimes it goes wrong."