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Explainer: Why does female fertility decline?

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Former Olympic swimmer Lisa Curry has announced she will undergo fertility treatment to try to have a baby with her partner of three years. News reports say doctors estimate she has less than a 10% chance of success.

Given her doctors also note Curry's ovaries are in "much better shape than expected", why is it that her chances of having a child through IVF are so low? After all, Curry already has three children, which shows she has been fertile. The main factor is her age – 51.

While age also affects male fertility (sperm quality decreases with age), men generate new sperm throughout most of their lives. A woman, on the other hand, is born with a finite number of oocytes (eggs) that start to develop soon after she is conceived.

Declining numbers

At birth, a girl will have approximately one million eggs but, through natural cell attrition, she'll have around 400,000 left by the time she reaches puberty. These eggs will have remained in a quiescent, dormant stage until the onset of puberty.

In response to hormone surges, one egg (on average) will undergo the final stages of growth and be ovulated approximately every 28 days for between four and five decades.

The ovum is unique for being the largest cell in the body and the fact

that can't be regenerated. By the time it has ovulated and is ready to be fertilised, it'll be at least a couple of decades old. Indeed, an ovum awaiting fertilisation can be up to 40 years old.

At peak fertility (between the ages of 17 and 25), a sexually active woman has a 20% to 25% chance of becoming pregnant each month. At 32, her fertility starts to decline and by 40, it has halved.

She now also has a higher risk of miscarriage, pregnancy complications, gestational diabetes and birth defects.

So what is happening?

Deteriorating function

We carry 46 chromosomes, with each parent contributing 23 of these. For this inheritance to go smoothly, eggs and sperm need to contain half the number of chromosomes as normal cells.

If sperm and eggs contained a full set of chromosomes (46), at the time of fertilisation, the resulting embryo would contain 92 chromosomes. Your parents contributing equal numbers of chromosomes also aids genetic variability (allowing you to inherit traits from both your mum and dad).

When the final stages of egg growth is triggered just before ovulation, it undergoes a process called meiosis. The main purpose of meiosis is to shed half the number of chromosomes in the egg (from 46 to 23). In order for meiosis to occur correctly, chromosomes are moved around the cell on scaffolding called spindles.

As women get older, the components of meiosis, including the expression of genes that control its rate, the spindles and other repair

mechanisms, deteriorate. This results in increasing numbers of eggs with incorrect numbers of chromosomes (this is called aneuploidy).

While most aneuploidies result in implantation failures (the inability for the embryo to embed in the uterine wall) or miscarriage, not all of them are lethal to the embryo. Incorrect numbers of chromosomes also result in Downs Syndrome, where a child has an extra chromosome 21.

Studies in mice have revealed that the rate of chromosome misalignments increases from 15% in young mice (six to eight weeks old, which is their peak fertility) compared to 50% in aged mice (12 months old).

Chromosome quality

The quality of the chromosomes themselves is also compromised by age.

Telomeres are structures that protect chromosomes from damage, similar to the plastic bit at the end of shoelaces. Shortening of telomeres is associated with cell ageing throughout the body, including ageing eggs.

Eggs have shorter telomeres from decades of inactivity. In comparison, telomere length within sperm is not affected as sperm-producing cells contain high levels of telomerase, the enzymes involved in repairing telomeres.

The ability of eggs to produce energy also decreases with age. All cells contain organelles called mitochondria that produce energy. Comparisons between aged and young mice show that ageing results in a 40% decrease in energy levels, 44% lower mitochondrial DNA and significant changes in the mitochondrial structure within the egg.

The combination of these and other factors, as well as the natural decline of the egg pool as women age, contribute to their decreasing fertility.

The introduction of the contraceptive pill, increased education and career opportunities have contributed to the increasing age of mothers.

Lisa Curry may have brought this issue into the spotlight but it is something that affects all of us, one way or another.

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