Researchers uncover secret of pregnancy problems in older women

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Scientists are a step closer to understanding why older women are more likely to produce abnormal eggs, increasing the risk of infertility, miscarriage and birth defects such as Down's Syndrome.

The research has been carried out against the backdrop of dramatically increased cases of Down's Syndrome pregnancy caused by the growing trend for women to postpone having babies until their late thirties and early forties.

While it has long been known that the increased risk of abnormalities in older women is due to eggs containing the wrong number of chromosomes, the underlying causes have remained a mystery. Research published today in the journal Current Biology sheds new light on why this happens.

The key is declining levels of proteins called cohesins, which hold chromosomes together by entrapping them in a ring. This is essential for chromosomes to split evenly when cells divide.

All the cells in the body, except for sperm and eggs, contain two copies of each chromosome. Sperm and eggs must lose exactly one copy in preparation for fertilisation. This halving of chromosome number involves a very complex form of cell division. In eggs the problem is compounded by the fact that the physical attachments that hold chromosomes together are established before birth and must be maintained by cohesins until the egg divides just before ovulation. In

humans this can take decades.

In a study, led by Dr Mary Herbert, and funded primarily by Newlife Foundation for Disabled Children, Infertility Research Trust, and the MRC, researchers at Newcastle University and Newcastle Fertility Centre used eggs from young and old mice to show that cohesin levels decline gradually as females get older.

This results in weakened cohesion between chromosomes and failure to divide equally during the halving of chromosome number in eggs of older females.

By tracking chromosomes during division in the egg, the Newcastle team found that the reduced cohesin in eggs from older females resulted in some chromosomes becoming trapped and being unable to divide properly.

Eggs that are defective in this way may fail to develop, resulting in infertility, or they may give rise to a pregnancy with a high risk of miscarriage, or to the birth of a baby with Down's Syndrome.

"Reproductive fitness in women declines dramatically from the mid-thirties onwards. Our findings point to cohesin being a major culprit in this," explains Dr Mary Herbert, Reader in Reproductive Biology at the Institute of Ageing & Health, who is based at Newcastle's Centre for Life.

"The aged mice we used are equivalent to a woman in her early forties. Cohesin levels were very much reduced in eggs from older mice and the chromosomes underwent a very messy division resulting in the wrong number of chromosomes being retained in the egg.

"The next step in this research will be to see if the same problem exists

in human eggs and to work out why cohesin is lost during female reproductive ageing. If we can understand this, we will be in a better position to know if there is any possibility of developing interventions to help reduce cohesin loss."

Dr Herbert stressed: "Undoubtedly, the best way for women to avoid this problem is to have their children earlier."

Provided by Newcastle University