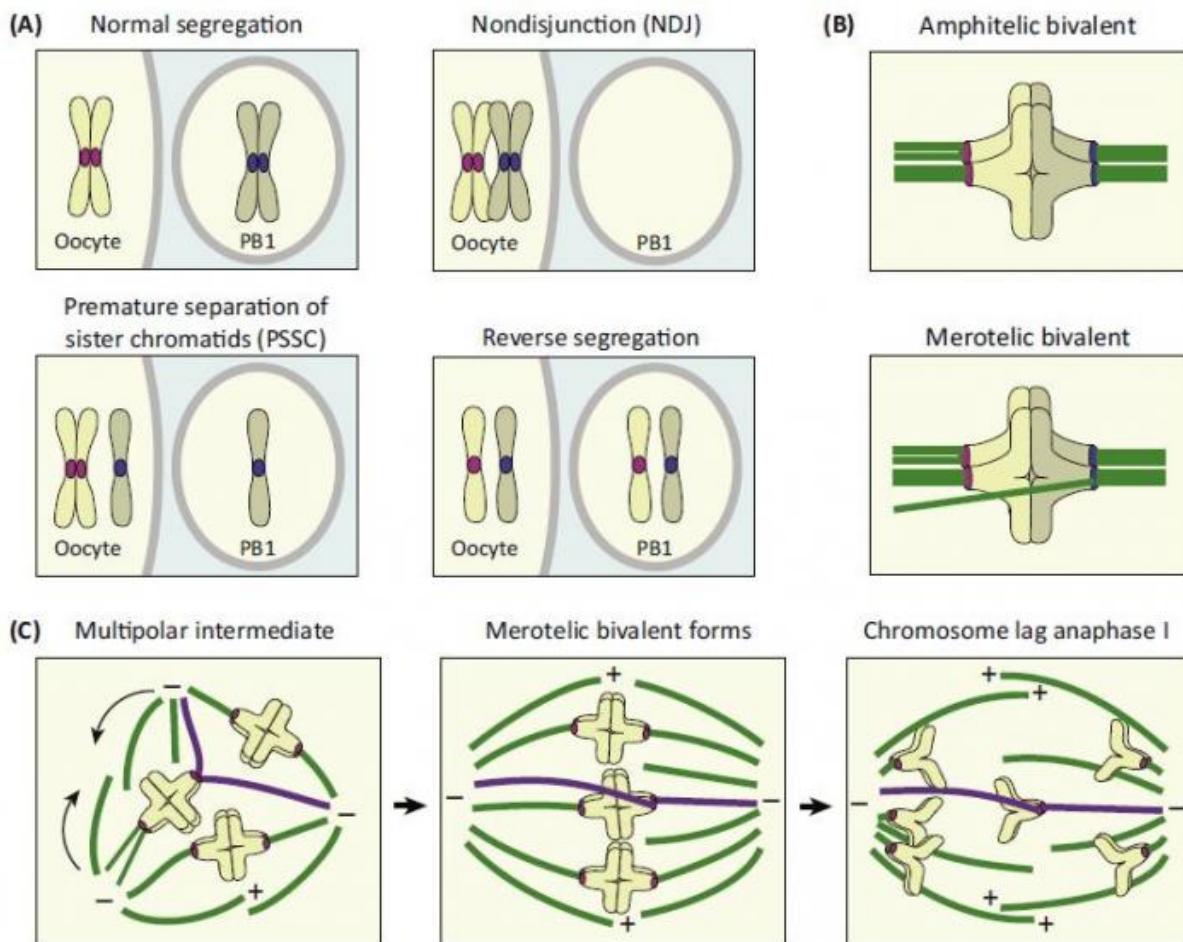


How human eggs end up with the wrong number of chromosomes

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This figure depicts chromosome segregation errors in meiosis. (A) The three main classes of segregation errors. (B) Incorrect alignment of chromosome kinetochores (C) Mitotic spindle errors. Credit: Webster and Schuh/*Trends in Cell Biology* 2016

One day before ovulation, human oocytes begin to divide into what will become mature eggs. Ideally, eggs are packaged with a complete set of 23 chromosomes, but the process is prone to error, especially with age. In a Review published October 20 in *Trends in Cell Biology*, researchers discuss the latest research on why many human oocytes frequently have a wrong number of chromosomes—which may lead to genetic disorders, such as Down syndrome and miscarriage.

"We're really interested in understanding what controls the segregation of chromosomes when an egg develops and where errors come from that could explain the high rate of eggs having an abnormal number of chromosomes," says Melina Schuh, Director of the Department of Meiosis at the Max Plank Institute for Biophysical Chemistry in Germany, who co-authored the paper with postdoctoral fellow Alexandre Webster.

Human oocytes pack the mother's DNA into 46 chromosomes. When they divide into eggs—a process called meiosis—these 46 chromosomes gather along the midline of the oocyte and are pulled in two directions by spindle fibers. The final product of meiosis is an egg cell with 23 chromosomes. Compared to other species, there is some evidence that [human eggs](#) are less able to monitor whether all chromosomes are correctly attached to the spindle fibers prior to segregation, independent of age. This leads to egg cells that unintentionally contain too few or too many (22 or 24) chromosomes—a condition known as aneuploidy.

Researchers have also found that oocyte spindle fibers are frequently unstable and may rearrange themselves during meiosis, which can last for up to a full day (much longer than other mammals, such as the mouse, for which egg maturation takes a few hours). The degree of spindle reorganization correlates with chromosome segregation errors.

Age-dependent causes of aneuploidy are more related to the

deterioration of the chromosome structure: "We found that as women get older that their chromosomes come apart before they are meant to separate from each other," Schuh says. "The points where spindle fibers attach to chromosomes (called kinetochores) also start to disintegrate with age, allowing [chromosomes](#) to orient in an abnormal way on the spindle, which is very likely to promote chromosome segregation errors."

At the moment, there is no way to therapeutically treat eggs with chromosomal abnormalities but there are tests to determine whether they are present in a fetus. Many countries offer non-invasive scans or, more recently, blood tests that can look for certain predictors of aneuploidy. For in vitro fertilization, clinicians know early on whether there are problems related to chromosomal segregation.

"Of course it can be emotionally very challenging to try to conceive or to go through different types of assisted reproduction," Schuh says. "But one positive aspect that came out of our studies is, although there is an average decline in oocyte quality as women get older, these women also still have many good [eggs](#) with no abnormalities."

More information: Alexandre Webster et al, Mechanisms of Aneuploidy in Human Eggs, *Trends in Cell Biology* (2016). [DOI: 10.1016/j.tcb.2016.09.002](https://doi.org/10.1016/j.tcb.2016.09.002)

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