Mammals put embryo development on hold

The ability to postpone embryo growth temporarily may be more widespread than previously thought.

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Humans may be able to temporarily suspend embryo development very early on in pregnancy.

Early embryos of all mammalian species might be able to pause their development, hitting play again only when conditions in the uterus are just right.

The ability of an embryo to go into 'diapause', a state of suspended animation after the egg is fertilized but before the growing ball of cells is implanted in the uterus, is relatively common in much of the animal kingdom. But it has been documented in less than 2% of mammalian species and never properly investigated in primates. This has led many researchers to speculate that it evolved independently in those mammals. A paper published this week in *PLoS ONE*[1] challenges that view, suggesting that all mammals may have this ability.

Researchers led by Grazyna Ptak, an embryologist at the University of Teramo in Italy, used as their baseline mice, one of the few mammals in which diapause is known to occur. In a mouse that has had its ovaries removed, the uterus is unreceptive and a mouse blastocyst will enter diapause, says Ptak. To this hostile environment, the team introduced blastocysts from sheep, which are not known to enter diapause, and saw the early embryos behave in exactly the same way as their mouse counterparts.

In as-yet unpublished work, the researchers have found that the same goes for rabbits and cows. "This strongly suggests that embryonic diapause has an ancient evolutionary origin," says Ptak. "As the physiology of the very early embryo is similar in all mammals, it's extremely likely that all mammalian species can do this."

The phenomenon is not more widely observed in mammals because it is no longer needed, she suggests. "If the female is living under controlled conditions with food, nice temperature and no overcrowding, she will never go through diapause because it's not necessary," Ptak says.

Pause for thought

Although the new paper makes no mention of humans, Ptak has considered the implications. In the 1990s, researchers at the National Institute of Environmental Health Sciences in Research Triangle Park, North Carolina, studied the development of human embryos in 189 naturally occurring pregnancies. For those that gestated for at least six weeks, implantation into the uterus occurred anywhere between 6 and 12 days after ovulation[2].

Ptak speculates that stress at around the time of conception, which can cause changes to hormone levels and so affect the receptivity of the uterus, could trigger diapause and help account for this variation. "Once the female is not stressed any more, the embryo will implant," she says.

Ptak also suspects that diapause could be behind a remarkable case study in which a woman undergoing *in vitro fertilization* seemed to experience a five-week delay from the collection of her eggs to the appearance of human chorionic gonadotropin (hCG), the hormone released once the embryo has implanted into the uterus[3]. The specialist involved in the case agrees. "I do think that a minor diapause is frequent in humans," says Jørgen Grinsted, a gynaecologist at Trianglen, a private fertility clinic on the outskirts of Copenhagen, Denmark.

If this turns out to be the case, Ptak thinks that the medical profession needs to take note. The due date for a baby is often worked out by counting on from the first day of the mother-to-be's last menstrual period. But if diapause is a regular feature of embryonic development in humans, this calculation will inevitably be inaccurate, which could lead to babies being wrongly classified as 'small for gestational age' and women undergoing Caesarean section before absolutely necessary, she says. "If the appearance of hCG and

hence implantation of the embryo were used instead of the menstrual cycle, due dates would be a lot more accurate and we would avoid a lot of obstetrical problems," she notes.

Juan Tarín, a physiologist at the University of Valencia in Spain, agrees that diapause probably does occur in human embryos and could help to explain the present inaccuracy in due dates[4]. "Certainly, hCG would be a better predictor of the expected delivery date than the date of last menstrual period," he says. But it is simply not practical to expect all women to test for a spike in hCG on a daily basis, he says

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References

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