NATURE | NEWS

First rodent found with a human-like menstrual cycle

The spiny mouse could one day aid studies of women's reproductive problems.

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The spiny mouse averages a 9-day menstrual cycle.

Mice are a mainstay of biomedical research laboratories. But the rodents are poor models for studying women's reproductive health, because they don't menstruate.

Now researchers at Monash University in Clayton, Australia, say that they have found a rodent that defies this conventional wisdom: the spiny mouse (*Acomys cahirinus*). If the finding holds up, the animal could one day be used to research women's menstruation-related health conditions.

"When you do science you're not surprised at anything — but wow, this was a really interesting finding," says Francesco DeMayo, a reproductive biologist at the US National Institute of Environmental Health Sciences in Research Triangle Park, North Carolina, who was not involved in the work.

The study, which was posted to bioRxiv preprint server on 3 June[1], involved 14 female spiny mice. The researchers found that the animals averaged a 9-day menstrual cycle and spent 3 days — or 20–40% of their cycle — bleeding. This ratio is similar to that in women, who typically bleed for 15–35% of their 28-day cycle.

To track the mice's periods, the team flushed the animals' vaginas with saline solution daily for 18 days. To ensure that the procedure itself did not cause the bleeding, the team treated five common lab mice in the same way. The scientists also dissected uteri taken from four spiny mice, each at a different stage of the menstrual cycle.

The team is continuing research into exactly how and when the mouse uterine lining breaks down and regrows. Jared Mamrot, a reproductive physiologist at Monash and a co-author of the study, has just sequenced the spiny mouse transcriptome — all of the RNA expressed by the animal's genes at a given time. This could provide information on how genes regulate different stages of the spiny mouse's menstrual cycle.

Similar or different?

Warren Nothnick, a researcher at the University of Kansas in Kansas City who studies the uterine-lining disorder endometriosis, says that it will take a lot of work to prove that the spiny mouse is a good model for human menstruation. But he is intrigued.

“There’s some really simple studies that they could do to see if these animals would develop endometriosis spontaneously,” he says. A finding that the animals do develop the disease naturally would be a major breakthrough, Nothnick adds.

The current animal model for endometriosis is the baboon, and primate research is expensive and time-consuming. Laboratory mice can be induced to menstruate, but only if their ovaries are removed and they are given abnormally large doses of hormones. Only 1.5% of mammals menstruate naturally, and most of them are primates.

The spiny mouse could also help to shed light on healthy menstrual function, DeMayo says. Scientists don’t know the source of the cells that repopulate the uterine lining after each menstrual cycle, he notes.

But DeMayo cautions that there is more to learn about how similar menstruation is in spiny mice and women, including the patterns of gene expression involved and how the hormones oestrogen and progesterone regulate the process in the mouse.

Study co-author Hayley Dickinson., a reproductive physiologist at Monash University, says that the mouse discovery was hiding in plain sight. Monash established a breeding colony of spiny mice in 2003, and later transferred the animals to the nearby Hudson Institute for Medical Research. When Dickinson's lab announced the menstruation discovery, several past students asked her how they could have missed it.

“The answer, as with many discoveries in science, is that no one really looked,” Dickinson says. “Everyone knew that rodents didn't menstruate.”

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References

1. Bellofiore, N. *et al*. Preprint at bioRxiv http://dx.doi.org/10.1101/056895 (2016).

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Majid Ali • 2016-06-17 01:28 AM

Menstruating Mice and Human Reproductive Health How will the discovery of menstruating mice help me with my work with gender-related problems of females of all ages? Prediction in any field is a risky proposition, and is especially so in biology. Still I cannot resist predicting something on the subject of men and mice. I predict that Australian spiny menstruating mice will enlighten me in my studies of : 1. Impact of respiratory-to-fermentative shift on reproductive health (ref.1,2), 2. Impact of altered states of gut microbiome and ecology on hormonal development of little girls (ref.3), 3. Impact of hyperinsulinism and raised blood testoterone levels in premenstrual girls (ref.4), 4. Dysmenorrhea and menstrual irregularities in teenagers (ref.5,6), 5. Facial skin changes of dryness, acne, pigmentation, and unwanted hair (ref. 5,6), 6. Cystless polycystic ovarian syndrome (ref.7), 7. Polycystic ovarian syndrome and endometriosis (ref. 8), 8. Infertility (ref.9), 9. Pseudomenopause (ref.10). Sugar, allergy, antibiotics, altered gut microbiome, chronic stress, insulin toxicity, and increased testosterone activity set the stage for the clinico-pathologic entities listed above. The order of the development of these entities as listed above is essentially correct. This is the main lesson my female patients across the full age spectrum have taught me. Biochemical and clinical observations that support the above relationships have been documented in the included citations. I am not uneasy in predicting that Australian menstruating mice will validate these lessons. So I am grateful to Bellofiore et al for discovering menstruating mice (ref.10). Like all cautious observers, they included the following in their paper: The spiny mouse is the first rodent species known to menstruate and provides an unprecedented natural non-primate model to study the mechanisms of menstrual shedding and repair, and may be useful in furthering our understanding of human specific menstrual and pregnancy associated diseases. I think time will prove them right. The relationships between pediatric ailments and menstrual disorders are generally recognized well on clinical grounds in the integrative medicine communities. This is not so among clinicians who do not sharply focus on the matters of addictive sugar intake, undiagnosed and untreated mold and food allergy, eczema, asthma, and frequent use of antibiotics administered for sore throats, otitis media, and common skin infections during the early years of life. The connectedness of these childhood disorders with later menstrual and endocrine disorders, such as polycystic

ovarian disorder, becomes evident when laboratory tests are done for allergy (Ig-E antibodies with specificity for mold, pollen, and foods), Krebs cycle metabolite (succinate and others), and toxic urinary compounds (arabinose, furan compounds, and others). In the context of complex gonadal, endocrine, and metabolic disturbances in females of all age groups, I foresee that menstruating spiny mice will also be equally suitable models. This will resolve the differences in opinions of integrative clinicians and doctors who largely limit themselves to standard pharmacologic therapies at this time. References 1. Ali M. Respiratory-to-Fermentative (RTF) Shift in ATP Production in Chronic Energy Deficit States. Townsend Letter for Doctors and Patients. 2004;253:64-65. 2. Ali M. Darwin, Dysox, and Disease. Volume X. The Principles and Practice of Integrative Medicine 3 rd. Edi. (2009) New York. Institute of Integrative Medicine. pp 189-226. 3. Ali M. Altered States of Bowel Ecology. (monograph). Teaneck, NJ, 1980. 4. Ali M. Beyond insulin resistance and syndrome X: The oxidative-dysoxygenative insulin dysfunction (ODID) model. J Capital University of Integrative Medicine. 2001;1:101-141. 5. Ali M. Oxidative menstrual dysfunction. Complementary Medicine Journal. 2000.6:17-23. 6. Ali M. The dysox model of adrenal dysfunction and gender devolution. Townsend Letter – The Examiner of Alternative Medicine. 2008;305:117-121. 7. Ali M. Cystless polycystic ovarian syndrome. http://insulininstitute.org/pcos_cystless.htm 8. Ali M. Amenorrhea, oligomenorrhea, and polymenorrhea, in CFS and fibromyalgia are caused by oxidative menstrual dysfunction. J Integrative Medicine. 1998;4:101-124. 9. Ali M. The unifying dysox model of hormone disorders and receptor restoration therapy. Townsend Letter – The Examiner of Alternative Medicine. 2007;291:145-151. 10. Bellofiore N, Ellery SJ, Mamrot J, et al. First evidence of a menstruating rodent:the spiny mouse. Preprint at bioRxiv. Doi: http://dx.doi.org/10.1101/056895