UC SANTA BARBARA

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Old Foes, Old Friends

Humans and hookworms have had a complicated relationship since the first day we stepped barefoot in the equatorial regions where the little parasites are endemic. Hookworms infect humans through skin contact. Larvae travel through the circulatory system before attaching to the small intestine, where they mature and feed on tissue and blood. The result: anemia, a deficiency in red blood cells.

The consequences of hookworm infection are well known. Anemia affects more than 40% of pregnant women globally, with 25% of pregnant women infected with hookworm (species *Necator americanus* and *Ancylostoma duodenale*). Though hookworm and other intestinal worms are usually associated with tropical regions of the developing world, the U.S. South was infested with hookworm up through the 20 th century. Despite hookworm affecting upwards of 750 million people worldwide, little is known about the interactions between hookworm and pregnancy or the effects on maternal and fetal health.

A paper in the American Journal of Human Biology led by UC Santa Barbara scholars investigates the relationship between hookworms and pregnancy in indigenous Tsimane women of the Bolivian Amazon. The Tsimane are forager-farmers who live in a tropical rain forest environment, and so are exposed to many diverse pathogens — including endemic hookworm. Tsimane women also have high fertility — the average woman has nine births over her lifetime. By analyzing longitudinal data, the researchers sought to determine if there's a tradeoff between mounting an immune response to hookworm and having a successful pregnancy.

"Hookworm is such a common infection in many parts of the world and it's a really ancient infection," said Amy S. Anderson, a UC Santa Barbara anthropology doctoral student and lead author. "And so it's one that in a certain sense, our immune systems have become quite tolerant towards. But the way that our immune system shifts when we're tolerating a chronic hookworm infection has some similarities with the way our immune system needs to tolerate the non-self that is a fetus growing during pregnancy."

As Anderson explained, a fetus is like a foreign organism that the mother's body has to both recognize as such and tolerate to sustain a successful pregnancy. Because hookworms and fetuses share immunological characteristics, the papers' authors hypothesized that changes in maternal immunity aimed at ensuring fetal tolerance may dampen immune responses to hookworm during pregnancy. They wondered if as a result, pregnant women might be more susceptible to new hookworm infections and higher morbidity, especially anemia, from existing infections.

To test their hypothesis, the researchers analyzed a mix of cross-sectional and longitudinal data on hemoglobin, hookworm infection, several markers of parasite-induced inflammation, and whether a woman was pregnant and in which trimester. Their findings, though preliminary, show some support for the hypothesized interaction between pregnancy and hookworm infections: pregnant women are slightly more likely to experience hookworm infection, and possibly worse health effects of that and other infections she may be exposed to during pregnancy.

"The effects are small," Anderson said, "and mostly concentrated in the first trimester, especially the excess hemoglobin loss and immune modulatory changes. But they support the idea that immune shifts in the first trimester navigate a slight trade-off between responding to hookworm infection and tolerating a fetus, because a first-semester fetus is more likely to get caught in 'friendly fire' from mom's immune system. In the eyes of the immune system, the cluster of [fetal] cells at the beginning of pregnancy appears to have more similarities to parasites like hookworm than a third-trimester fetus does."

Further, Anderson said, the findings "indicate that we may want to keep a closer watch on pregnant women in their first trimester, because we don't know what the long-term implications of a woman's first trimester disruptions are on her or her child's health down the line."

As Michael Gurven, a senior author on the paper and professor of anthropology at UCSB, explained, "Consequences of hookworm infection on pregnancy and immune function, and of pregnancy on infection and immunity — this is unexplored territory. Yet pre-natal exposures are now recognized as having lots of different downstream health impacts across the life course.

"The role of our wormy 'old friends' in modulating immune function in ways that don't just harm — but might even protect — against certain chronic conditions is also changing how we think about infection," Gurven continued. "We still have much to learn about the health ecology of mom, baby and worms, and this study is just the beginning."

Also contributing to the paper were <u>Carmen Hové</u>, a UCSB doctoral candidate in anthropology, and <u>Thomas S. Kraft</u>, a UCSB anthropology postdoctoral scholar.

About UC Santa Barbara

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