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How Sweet It Isn't

Can a mom's intake of artificial sweeteners while pregnant make her child obese?

One day soon, a pregnant woman ordering a diet soft drink may elicit the same disapproving looks as if she had asked for a Scotch. As researchers continue to learn about the effects of sugar substitutes on health, diet drinks may join caffeine, raw fish and alcohol on a growing list of foods and drinks to avoid during pregnancy.

Recent studies have raised concerns about the association between artificially sweetened beverages (ASBs) and premature birth. In 2016, Dr. Meghan Azad, a young scientist at the University of Manitoba, hoisted another cautionary flag when she discovered that women who consumed one or more ASB per day during pregnancy were twice as likely to have a child who is overweight at one year of age, compared to women who avoided these beverages.

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Dr. Meghan Azad, Assistant Professor University of Manitoba

"Typically, we think of sugar as the 'bad guy,'" says Dr. Azad, an assistant professor in the Department of Pediatrics & Child Health at the University of Manitoba and a research scientist at the Children's Hospital Research Institute of Manitoba. "It turns out that replacing sugar with artificial sweeteners in pop, or even in coffee and tea, may not be such a good idea. If a mom consumes diet drinks on a daily basis during her pregnancy, it may lead to—of all things—obesity in her infant."

If it happens in mice…

As often happens in health research, Dr. Azad drew inspiration from animal studies. She took a particular interest in a 2014 study published in the journal *Nature*, which showed that giving artificial sweeteners to mice upset the normal balance of microbes in their guts. This disruption altered the way the mice metabolized sugar, eventually causing them to develop glucose intolerance—a pre-diabetic state in which the blood glucose is raised beyond normal levels.

At the time, Dr. Azad was mining data from AllerGen's CHILD Study (CHILD). Specifically, she was studying how various exposures during pregnancy and early life affect the gut bacteria of human infants, and whether or not those bacterial shifts lead to the development of chronic diseases, like asthma, allergy and obesity, down the road.

"CHILD is like a massive jigsaw puzzle," she says of the national project that has been following 3,500 Canadian children from before birth, tracking nearly every aspect of their health and development. "We are constantly looking at the babies' exposures during pregnancy and in infancy—like whether the mom had a caesarean section or vaginal delivery, what type of diet the baby was fed, whether the mom or baby received antibiotics, if there was exposure to household dust and mould, and even whether siblings or pets were present in the home—to try and pinpoint the environmental factors affecting gut bacteria."

After reading the *Nature* article, Dr. Azad wondered: Could a mom's consumption of ASBs during pregnancy affect her baby's weight? "Some animal research has suggested that consuming artificial sweeteners during pregnancy can predispose offspring to obesity, but we didn't know of any human studies looking at this outcome," she says. To answer the question, Dr. Azad went back to CHILD.

Mothers involved in the study had provided detailed information on what they ate and drank during pregnancy—including ASBs—and their children are regularly weighed, measured, and tested by CHILD researchers as they grow. As it happened, almost one in three CHILD mothers had consumed ASBs during pregnancy.

Comparing the moms' dietary patterns to their babies' physical development, Dr. Azad and her team generated one immediate finding: ASB consumption in pregnancy had no effect on the infants' weight at birth.

A deeper dive into the data, however, revealed something of interest: By the age of one, the children of moms who drank ASBs every day during pregnancy had twice the risk of being clinically overweight—defined as a body mass index (BMI) above the 97th percentile—compared to those born to moms who avoided ASBs altogether. "This suggests that a mom's ASB consumption influenced her baby's weight gain after birth, rather than during fetal growth," says Dr. Azad. "This association persisted whether the artificial sweeteners came from soft drinks, coffee or tea."

Filtering out the noise

In theory, the ASB consumption could mask another culprit. As Dr. Azad points out, "it is conceivable that pregnant mothers who drink ASBs go on to feed their babies more unhealthy foods, which could explain the extra weight gain by the babies' first birthdays." Or these moms may weigh more than average and pass on their genetic tendency for obesity to their children.

To make sure they had considered all of these variables, Dr. Azad brought in Dr. Russell de Souza, a nutritional epidemiologist from McMaster University, and Dr. Atul Sharma, an expert on infant growth curves from the University of Manitoba, to review the data. The team also factored socioeconomic status, maternal weight, total caloric consumption, and quality of the diet into the analysis. The link between ASBs and baby weight at one year of age held up. To Dr. Azad's knowledge, "this is the first human evidence that consumption of ASBs during pregnancy may influence a baby's BMI."

One might ask: What's wrong with a bit of extra baby fat? Aren't squirrel cheeks part of what makes babies so adorable? As several previous studies have shown, however, "excess weight early in life predicts obesity later in childhood and even

in adult life," says Dr. Azad, who plans to track the children's weight as they grow to see if the trend towards obesity persists.

I can relate to that

Dr. Azad's study illustrates CHILD's scope and versatility. "No one had the link between ASB and baby weight in mind when CHILD was launched in 2008, and yet when we considered this question years later, we were able to answer it by looking at CHILD data," she says. "CHILD is an incredibly powerful tool."

The results of Dr. Azad's research, published in *JAMA Pediatrics* in 2016, ignited massive media interest. Within days of publication, she was giving interviews across North America, and even appeared in an Australian documentary TV show. "It seems that having babies and drinking diet beverages are things that everyone can relate to," she says.

Her findings popped up in dozens of print articles, with some headlines making exaggerated and misleading claims such as "sugary beverages during pregnancy cause childhood obesity," or warning moms against making the "diet mistake that could make your kids overweight for life."

The truth, says Dr. Azad, is far less clear-cut. For one thing, pregnant women who drank ASBs less often than once a week did not have heavier one-year-olds than other women—it was only more frequent consumption that put babies at increased risk. More fundamentally: "It's very difficult to prove cause and effect. Our study has just exposed a link."

To demonstrate that ASBs actually cause weight gain, researchers will need to show how the ASBs act in infants' bodies. In this regard, Dr. Azad has several theories to explore.

Looking for an explanation

The first theory involves alterations in the gut microbiome, which mothers transmit to their children during birth. "We know that gut bacteria influence how much energy we absorb from food, and if you compare the microbiomes of obese and lean individuals, you will see differences," she explains. It is possible that the ASBs consumed by pregnant women favour the growth of more obesity-inducing bacteria in their guts. When the mothers transmit this "obesity-prone" microbe profile to their babies, the babies go on to gain weight.

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Her second hypothesis has to do with metabolism. The human body has a programmed response to sugar, including the release of insulin and other hormones. But it's not just sugar that triggers this cascade—the perception of sweet taste can also set one's biochemical gears in motion. According to Dr. Azad, some evidence suggests that "routine consumption of artificial sweeteners may confuse and 'reprogram' our metabolism in a way that favours weight gain."

Along a similar line, early exposure to ASBs may orient babies toward sweet-tasting things, including foods with real sugar. In fact, researchers have observed this phenomenon in mice. "If mice are exposed to artificial sweeteners as babies, they're more likely to choose Froot Loops over regular mouse food when they reach adulthood," says Dr. Azad. Currently, she is planning a study to see if an even earlier exposure to ASB—while mice are still in the womb—will produce a similar "sweet tooth."

A media focus on sugar as a food to avoid has led many people to resort to artificial sweeteners as a substitute, says Dr. Azad. While Health Canada has stated that: "Consumption of sugar substitutes during pregnancy does not pose a health risk," Dr. Azad's research builds on a body of evidence suggesting there may be more to this story.

Until further research provides more definitive answers, Dr. Azad advises pregnant women to think twice before reaching for that can of Coke Zero. "It does no real good and, if it becomes a habit, could potentially be harmful. When you're pregnant, unsweetened drinks like water are the best option," she says.