Scientists seek origins of obesity in the womb

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In this photo taken Oct. 8, 2009, Kathy Perusse, center, poses for a photograph outside her home with two of her children, David Laflamme, 16, left, and Anne-Marie Laflamme, 22, in Trois-Rivieres, Quebec. (AP Photo/The Canadian Press, Paul Chiasson)

(AP) -- When Kathy Perusse had weight-loss surgery and shed 120 pounds, she may have done more than make her own life easier.

She went on to have two daughters, and she may have boosted their chances of avoiding becoming obese, like her two older children are.

That's the implication of research suggesting that something in an obese woman's womb can program her fetus toward becoming a fat child and adult. It's not about simply passing along genes that promote obesity; it's some sort of still-mysterious signal.

The idea has only recently entered conversations between doctors and female patients, and scientists are scrambling to track down a biological explanation. That knowledge, in turn, may provide new ways to block obesity from crossing generations.

While there's some disagreement on how important the womb signal is, "the evidence is building and building that it is a substantial issue," said Dr. Matthew Gillman of Harvard Medical School, who studies prevention of obesity.

Others agree. "I think it could be a hugely significant factor," said Robert Waterland of the Baylor College of Medicine in Houston, who studies the effect in mice.

Dr. Rudy Leibel, an obesity expert at Columbia University, says he doubts it plays a huge role, but still believes it's worth studying. If scientists can uncover its biological underpinnings, he said, they may be able to use that knowledge to prevent or treat obesity from other causes.

Perusse, 39, of Three Rivers, Quebec, knows the effects of being very fat. Before her weight-loss surgery in 1995, she packed 284 pounds on her 5-foot-2 frame. She could not ride a bike or climb stairs to her second-floor home without stopping to rest.

Now, although she's still overweight, those limitations are history, she said through an interpreter.

But her older children struggle with their weight. At 5-foot-3 and 300 pounds, her 22-year-old daughter can't bathe her own two children, Perusse said. Her 16-year-old son weighs 230 pounds and stands 5-foot-6.

They were born before she had the weight-loss surgery. Her two younger

daughters, ages 4 and 7, came along afterward. Their weights are normal so far, though Perusse said her older children weren't overweight at those ages either.

So she's using diet and exercise to try to protect them against what she called rotten genes, including those from their 400-pound father. She said she isn't optimistic.

But Dr. John Kral of the SUNY Downstate Medical Center in New York says his research suggests that obese women who lose weight before pregnancy may be helping the next generation keep off excess pounds - even if fat-promoting genes run in the family.

With researchers at Laval Hospital in Quebec, Kral has studied children of severely obese women who were born before or after their mother's weight-loss surgery. They found that, in comparison to children born before surgery, those born afterward were far less likely to be severely obese.

In addition, those born afterward showed lower levels of blood fats and indicators of future diabetes.

Kral says families typically don't change lifestyle or diet after surgery, so that doesn't explain the outcome.

Instead, he says, the surgical bypass operation made the women's bodies less efficient at digesting and absorbing food, and lowered levels of sugar and fat in the blood. That, in turn, would reduce the number of calories delivered to the fetus to levels like those provided by a normal-weight mother, he said.

And the women's shedding of pounds before the pregnancy would also help, he said.

While scientists are still trying to explain just how obesity could be transmitted from the womb, it makes sense that a mother's obesity could affect her children's long-term weight, Waterland said. Cues in early life, including some in the womb, guide the development of a person's brain circuitry for controlling the balance between calories consumed and those burned away, he said. So a signal there could have a long-lasting impact.

Or, maybe such a signal predisposes the child to make more fat-storing cells, others said.

It's still not clear just what in the womb could create such effects - high levels of blood sugar and certain fatty acids are some leading candidates.

Waterland has found evidence it may have to do with how critical genes are regulated. Chemical tags attach to the chromosomes and act like dimmer switches to modulate how hard certain genes work.

Waterland studied mice genetically prone to porkiness and found the fatter the mom, the heavier her offspring tended to be. But that effect was blocked when researchers fed pregnant mice a cocktail of substances that encourage the chemical tags to attach to the chromosomes.

What does that suggest? Maybe a mom's obesity somehow interferes with the regulation of certain genes, and the chemical cocktail overcame that, Waterland says.

Those genes might affect the offspring's long-term weight if they're involved in the brain's regulation of appetite and activity levels, Waterland proposes. He also says it's too soon to tell whether an obesity-blocking supplement could work in women as well as in the mice.

Once scientists identify the obesity signal, they may be able to recommend ways to suppress it, perhaps through diet or behavioral strategies.

In the meantime, experts say, obese women can take their own steps.

- Avoid pregnancy until you've lost weight. That's wise anyway, since obesity in pregnancy raises the risk of complications like diabetes, cesarean deliveries and stillbirth.

- If pregnant, hold down the weight gain during pregnancy. The Institute of Medicine recently recommended that an obese woman gain 11 to 20 pounds, rather than the 25 to 35 pounds allowed for healthy women of normal weight.

- After giving birth, get down to a healthy body weight to prepare for the next pregnancy.

Dr. Laura Riley of Massachusetts General Hospital in Boston said she gets her patients' attention when she tells them their obesity could promote the same problem in their children.

"I'm a mother," Riley added. "Believe me, it caught my eye."